American Journal of Diseases of Children

VOLUME 44 AUGUST, 1932 NUMBER 2

FUNCTION OF THE LIVER IN SCARLET FEVER

S. VAN CREVELD, M.D.

AMSTERDAM, HOLLAND

Among the various acute infectious diseases in which the study of the function of the liver is of great importance in the beginning and during the further course of the disease, scarlet fever takes a prominent place. During the acute fever stage of this condition there are generally several clinical indications of disorder of this function. After this acute stage of the fever involvement of different organs may occur, and though some organs may be especially preferred one may say that all parenchymatous organs can be affected, including the liver. In consultation with Dr. Herderschee, chief of the department of infectious diseases of the Wilhelmina Hospital, I therefore decided to make a further study of the function of the liver in scarlet fever, not only during the acute stage of the fever, as has been done until now, but during the further course of the disease when nearly all of the clinical symptoms have disappeared.

The methods generally used for the study of the function of the liver are those based on the excretion of certain dyes and the behavior of the liver with regard to certain carbohydrates, especially galactose and fructose. The use of intravenous injections of the commonly employed dyes in children is still limited and *a priori* not wholly without danger. As I tested mostly children between 6 and 12 years of age, I did not use this method, but studied the function of the liver principally with regard to the carbohydrate metabolism.[1]

In connection with the significance of the liver in water metabolism, the different carbohydrates were always given in the same quantity of water (a small glassful), thus making it possible also to study the excretion of water during scarlet fever. All experiments were done in the morning on patients who had not received food for sixteen hours.

EXPERIMENTS WITH FRUCTOSE

It is known that the liver function test with fructose gives a positive result, especially in diffuse parenchymatous diseases of the liver.

From the Department of Infectious Diseases, Wilhelmina Hospital, and the Laboratory for General Pathology, Town University of Amsterdam.

1. Harris (J. Clin. Investigation **4**:211, 1927) investigated liver function with the dye test in adult patients with scarlet fever during the acute fever stage, but he did not find deviations.

Strauss' original test of hepatic function has been modified so that at present the analysis of the change in the total amount of sugar and in the fructose content of the blood after the ingestion of fructose has at least the same importance as the examination of the urine after the ingestion of sugar.[2] This is especially true when, as is often the case in scarlet fever, there is a disturbance of the function of the kidney, which *a priori* might prevent the excretion of sugar (Schirokauer[3] and others).

On the basis of results in healthy children and in children with diseases of the liver I generally gave from 30 to 45 Gm. of fructose. The large quantities of fructose (from 80 to 100 Gm.) that earlier investigators gave and that in children often caused vomiting and diarrhea are superfluous, especially since a simultaneous examination of the blood is made.

Incidentally, some investigators have used these large quantities in examining patients for their tolerance for fructose in the beginning of scarlet fever. W. Schmidt,[4] for example, found a decreased tolerance for fructose in seven adults with scarlet fever as long as the urobilinuria existed. In thirteen children examined during the second half of the first week of scarlet fever, after the ingestion of 100 Gm. of fructose (in children less than 6 years of age, from 50 to 75 Gm.) Tachau[5] found a slight excretion of fructose in the urine in only four cases. In patients with scarlet fever Fleischer and Takeda[6] never obtained a positive Seliwanoff reaction after the ingestion of fructose. In a recent investigation von Kostyál and Takács,[7] after giving 50 Gm. of fructose in eight cases of scarlet fever, did not find an excretion of sugar either at the beginning of the disease or six weeks later.

Experiments with fructose were performed by me in thirty-five cases. In nineteen cases the experiment was done for the first time on the third, fourth or fifth day of the illness, when urobilinuria was nearly always present, and then was repeated once a week until the fifth week after the beginning of the illness. Each time a total blood sugar curve was made, and one hour after the ingestion of fructose the fructose content of the blood was determined.

---

2. Snapper; Grünbaum, and van Creveld: Arch. f. Verdauungskr. **38**:1, 1926. van Creveld and Ladenius: Ztschr. f. klin. Med. **107**:328, 1928. van Creveld: Klin. Wchnschr. **6**:697, 1927.

3. Schirokauer: Ztschr. f. klin. Med. **78**:462, 1913. The very high fasting blood sugar values without glycosuria found in some cases of scarlet fever may also be cited in this relation (Andresen, J., and Schmidt, A.: Klin. Wchnschr. **6**:213 (Jan. 29) 1927.

4. Schmidt, W.: Deutsches Arch. f. klin. Med. **100**:786, 1910.

5. Tachau, P.: Leberinsuffizienz bei Scharlach, Jahrb. f. Kinderh. **77**:534, 1913.

6. Fleischer and Takeda: Deutsche med. Wchnschr. **37**:1650, 1911.

7. von Kostyál and Takács: Ztschr. f. Kinderh. **50**:243, 1930.

In fifteen other cases the tolerance for fructose was investigated only once for the period from the third to the fifth day of illness. In the remaining ten cases this test for tolerance was performed once during the first period of the illness and was repeated at the end of the third or at the beginning of the fourth week, as at this time most complications of scarlet fever occur.

In table 1 the detailed results of a number of these experiments are given. In resuming the results of all the experiments with fructose I

TABLE 1.—*Results of Tests with Fructose at Different Stages of Scarlet Fever After the Beginning of the Disease*

Case	Day of Illness	Fructose Ingested, Gm.	Blood Sugar, per Cent: Fasting	After ½ Hr.	After 1 Hr.	After 1½ Hr.	Maximal Rise of Blood Sugar, Mg. per 100 Cc.	Fructose Content of Blood After 1 Hr., Mg. per 100 Cc.	Urinalysis: Fehling Test	Optical Rotation	Seliwanoff Test
1	6	30	0.0985	0.124	0.122	0.120	25.5	0.015	—	Inactive	+
	13	30	0.095	0.113	0.101	0.105	18.0	0.012	—	Inactive	Trace +
	20	30	0.081	0.108	0.098	0.091	27.0	0.008	—	Inactive	+
	27	30	0.082	0.101	0.100	.....	18.0	0.018	—	.....	Trace +
2	10	30	0.079	0.092	0.090	0.087	13.0	.....	—	.....	Trace +
	17	30	0.0765	0.0825	0.095	0.080	18.5	0.008	—	.....	Trace +
	24	30	0.069	0.090	0.082	0.083	21.0	0.009	—	.....	+
3	4	30	0.102	0.127	0.112	0.102	25.0	0.008	—	.....	—
	11	30	0.087	0.101	0.095	0.084	14.0	.....	—	.....	+
	18	30	0.095	0.1015	0.0895	0.0905	6.5	.....	—	.....	Trace +
	25	30	0.0835	0.093	0.084	0.087	9.5	.....	—	.....	..
4	4	30	0.095	0.119	0.125	0.110	30.0	0.012	—	.....	+
	11	30	0.087	0.0995	0.091	0.089	12.5	0.014	—	.....	Trace +
	18	30	0.0805	0.1065	0.1025	0.0935	26.0	.....	—	.....	+
	25	30	0.0825	0.112	0.0955	0.0845	29.5	.....	—	.....	+
5	6	30	0.072	0.087	0.092	0.077	20.0	0.012	—	.....	+
	13	30	0.092	0.115	0.110	0.107	23.0	0.006	—	.....	+
	20	30	0.079	0.088	0.080	0.068	9.0	0.008	—	.....	+
	27	30	0.092	0.115	0.107	0.087	23.0	0.007	—	.....	..
6	16	45	0.088	0.106	0.116	0.102	28.0	0.012	—	Inactive	Trace +
7	21	45	0.082	0.104	0.097	0.083	22.0	0.014	Trace +	+0.06°	Trace +
8	15	45	0.086	0.106	0.115	0.102	29.0	0.008	—	Inactive	+
9	21	45	0.097	0.123	0.098	0.086	26.0	0.004	—	Inactive	..
10	5	45	0.093	0.112	0.105	0.102	19.0	0.004	Trace +	Inactive	..
11	5	60	.....	.....	.....	.....	....	0.012* 0.009†	Trace +	−0.12°	+

* After three-fourths hour.
† After one-half hour.

can say that in no case could an excretion of any importance be found either during the first days of the illness, when urobilinuria, a palpable liver, etc., nearly always were present, or during one of the following weeks of the illness. Even in those experiments in which from 45 to 60 Gm. of fructose was ingested, the urine did not reduce or only slightly; it was optically inactive or showed only a slight deviation to the left, and the reactions that are more or less specific for fructose were only slightly positive. The blood sugar curve in this series of experiments did not differ from those obtained in healthy children after the ingestion of fructose. The total blood sugar content was never

higher than 0.127 per hundred cubic centimeters (a rise to more than from 0.135 to 0.140 per cent is abnormal), and the rise of the blood sugar content was always less than 30 mg. (a rise of at least 30 mg. is abnormal).[8] The fructose concentration of the blood, determined one hour after the ingestion of fructose, was never higher than normal, e. g., always less than 0.02 mg. per hundred cubic centimeters and, as a rule, even smaller than 0.01 mg.

EXPERIMENTS WITH GALACTOSE

One is accustomed to perform the galactose test for the determination of the function of the liver of adults, as introduced by Bauer, as follows: Forty Gm. of pure galactose is given in the morning, when the patient is fasting, and either the excretion of galactose in the urine within the first five hours or the changes in the blood sugar during

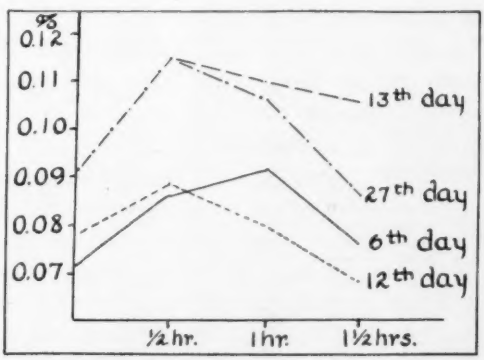


Chart 1.—Blood sugar curve in case 5 (table 1) on the different days of the disease.

several hours are determined. The excretion of more than from 1 to 2 Gm. of galactose, and, according to some investigators, of more than 1 Gm., in the urine is regarded as pathologic.[9] My own experience was in agreement with that of other investigators in that I found that in children between 6 and 12 years of age an investigation of the function of the liver may be made with much less than 40 Gm. of galactose. The smaller dosage is preferable because vomiting and

8. It is remarkable that von Kostyál and Takács, in investigating three cases of scarlet fever during the acute stage of fever found a very high rise of the blood sugar content after the ingestion of 25 Gm. of fructose. However, no clinical particulars of these cases are given. Was there perhaps a strong ketosis (see Tallerman, K. N.: Ketosis Accompanying Infections in Children, Am. J. Dis. Child. **30**:476 [Oct.] 1925)?

9. Dieryck, J.: La traversée comparée des monosaccharides en pathologie hépatique, Nutrition **1**:307, 1931.

diarrhea are avoided, and because the cost of the galactose for a large series of patients is not so high.

When the excretion of galactose in the urine was tested, I usually gave 25 Gm. of galactose, and in some experiments on adults, 40 Gm. When the blood sugar curve was made or, as has been done recently when the galactose content of the blood was estimated, I gave only 20 or 25 Gm.

It was necessary, however, to determine how much galactose was excreted in the urine within five hours after 25 Gm. of galactose had been taken in the morning by a number of healthy children who had not taken food for at least sixteen hours. In the greater number of these children galactosuria did not occur, and in the other children only slight galactosuria was present. However, in none of these control cases was the total excretion more than 0.7 Gm., and on the basis of

TABLE 2.—*Results of Galactose Test with 25 Gm. in Patients with Scarlet Fever and in Normal Children*

	Week of Illness	Number Tested	Patients Showing Excretion of More Than 0.7 Gm.		Patients Showing Excretion of More Than 1 Gm.	
			Number	Per Cent	Number	Per Cent
A. Scarlet fever group	1	93	25	28.89	17	18.28
	2	43	16	37.2	10	23.26
	3	53	24	45.28	16	30.2
	4	81	43	53.0	29	35.8
	5	21	11	52.0	7	33.0
B. Normal group: a maximum excretion of 0.7 Gm.						

these results I considered an excretion of 0.7 Gm. of galactose as the lowest pathologic limit.

Table 2 gives a short survey of the galactose tests performed on the children and on a number of children in different stages of scarlet fever; 0.7 Gm. and also 1 Gm. were chosen as the limit for a pathologic excretion. I found that in the first week of the illness only twenty-five of ninety-three patients investigated showed an excretion of more than 0.7 Gm.; the largest excretion was 2.61 Gm. (one case). Of the sixty-eight patients with an excretion smaller than 0.7 Gm., forty did not excrete any galactose in the urine. I further found in five children to whom I gave 40 Gm. of galactose on one of the first days of the illness an excretion of more than 0.7 Gm., in only two cases, namely, 1.63 and 1.13 Gm., amounts that are only slightly pathologic and that in adults would be only on the verge of a pathologic value.

A few facts must be mentioned regarding these galactose tests performed on the third to the fifth day of the illness. 1. As to the temperature of the patient on the day of the experiment and on the immediately succeeding days: I could not find any relation between

the quantity of galactose excreted and the rise of temperature; for example, a girl with a temperature of 40 C. (104 F.) did not show any galactosuria after the ingestion of 25 Gm. of galactose; further, a girl aged 13 years who had a temperature of 38 C. (100.4 F.) on the day of the experiment, and who had menstruated the day before, excreted only 0.48 Gm. of galactose following the ingestion of 40 Gm.

2. As to the quantity of urine that was formed during the first five hours after the ingestion of galactose: The quantity was usually rather small, as is often the case at the beginning of an acute illness with fever. There may have been some relation between this fact and the small amount of galactose excreted during the first days of the illness, but I did not find any. A small quantity of urine often contained much galactose, and in cases in which the diuresis was great I repeatedly found only a small excretion of galactose or none.

3. As to whether or not the patient had been given scarlet fever serum on one of the first days of the illness: Although I had expected to find considerable excretion of galactose by these patients, who at the beginning of their illness gave the impression of being seriously ill, I did not realize this expectation in the case of those in which 40 Gm. of galactose was given. An adult to whom 50 cc. of scarlet fever serum had been given three days before, following the ingestion of 40 Gm. of galactose, excreted 0.482 Gm. A child who had received scarlet fever serum two days before excreted 0.64 Gm. following the ingestion of 25 Gm. of galactose. Another child to whom 6,000 units of antidiphtheria serum had been given four days before excreted 0.368 Gm. of 25 Gm. of galactose ingested.

Table 2 reveals that the percentage of patients with a decreased tolerance for galactose increases after the first week of illness. The results of the tests performed during the third and fourth weeks of the illness interested me mostly. They showed that during these weeks the percentage of cases in which the excretion of galactose was larger than the limit in healthy children was considerably higher than that during the first week; several times the amount excreted was more than 2 Gm.; once I found an excretion of 3.8 Gm. By the fifth week the patients, as a rule, had been dismissed from the hospital, but in some cases during this week and even in the sixth and following weeks a pathologic excretion was found.

I did not find any definite relation between the existence of a complication in the third or fourth week of the illness (except in the cases of icterus, to be mentioned later) and a decreased tolerance for galactose. The following examples are given: One child with scarlet fever excreted no galactose after the ingestion of 25 Gm. on the day of his arrival in the hospital. During the third week of his illness nephritis developed; during the fourth week, when the nephritis was

still present, a repetition of the galactose test showed an excretion of only 0.4 Gm. Another patient with swelling of the glands excreted 0.263 Gm. during the fourth week; still another patient, 0.6 Gm. On the other hand, two other patients with swelling of the glands showed excretions of 1.44 and 2 Gm., respectively.

In a number of galactose tests I also examined the changes in the blood sugar content. Under normal circumstances the blood sugar curves after galactose show little variation from the fasting value. With an increase of the total blood sugar content one also finds an increased excretion in the urine.

In table 3 are recorded the highest values for the blood sugar content, with the corresponding average amount of galactose excreted in the urine, in nine children with scarlet fever in whom a galactose test

TABLE 3.—*Maximal Value of the Blood Sugar Content and the Simultaneous Excretion of Galactose in the Urine in Different Weeks After the Beginning of Scarlet Fever*

Blood Sugar Content, per Cent	Number Tests	Mean Excretion of Galactose, Gm.
0.1 –0.11	6	0.168
0.11–0.12	3	0.27
0.12–0.13	8	0.546
0.13–0.14	6	1.023
0.14–0.15	4	1.002
0.15–0.16	4	1.654
0.16–0.17	1	2.152
0.17–0.18	1	1.852
0.18–0.19	..	.....
0.19–0.20	1	1.786
0.20–0.21	1	2.395

with 25 Gm. of galactose was performed each week for the first four weeks of illness. It appeared that when the blood sugar content remained smaller than 0.13 per cent, the excretion of galactose was also small; when the blood sugar content rose to from 0.13 to 0.15 per cent, the excretion of galactose in the urine, with a single exception,[10] was considerable. In those cases in which a high galactosuria was found, the blood sugar content also appeared to have risen, without exception, to more than 0.15 per cent. Therefore the possible influence of a renal factor, which *a priori* must be reckoned with in scarlet fever —not rarely is there an accompanying nephritis—could not be established in these experiments following a comparison of the blood sugar curves after the ingestion of galactose and of the excretion of galactose in the urine.

10. This exception was in patient B, chart 2, in the third week of the illness: The blood sugar rose to 0.142 per cent, whereas the excretion of galactose remained less than 0.7 Gm.

The frequency of a pathologic rise in the blood sugar content after the ingestion of galactose during the different weeks of the disease did not differ from the frequency of a pathologic excretion of sugar in the urine.

In a number of patients I tried to make a closer investigation of the function of the liver in scarlet fever as regards the transformation and fixation of the galactose, by determining the galactose content of the blood. To determine the galactose content I made use of the observations of Somogyi:[11] When blood or deproteinized blood is

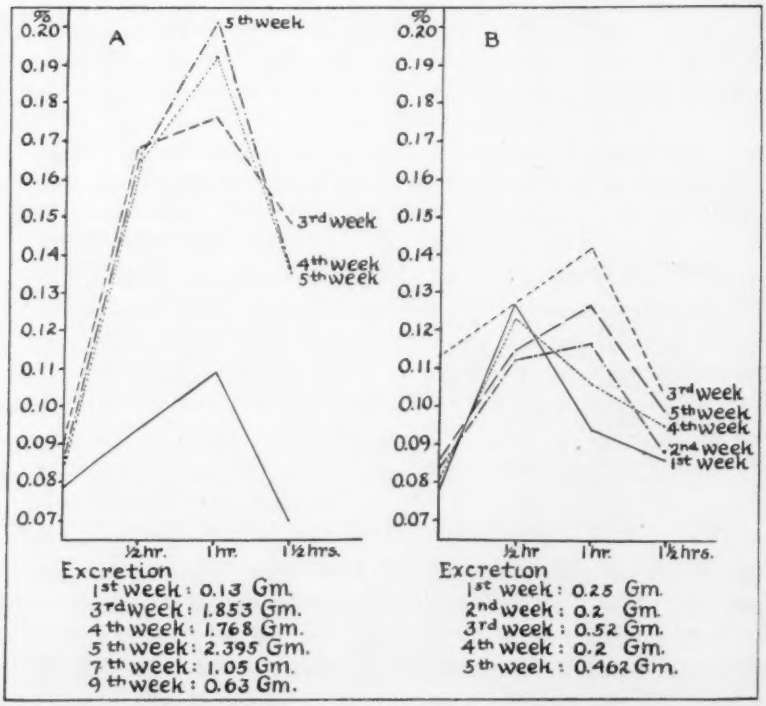


Chart 2.—Blood sugar curves of two patients (table 3) in different weeks of their illness.

shaken for a short time with washed yeast, all the dextrose in the blood is quickly absorbed. The remaining reducing substances of the blood, together with the galactose present, can be determined after centrifugation and removal of the yeast. If, therefore, the nondextrose fraction, or the so-called rest reduction, is determined in the blood of the fasting patient, and this determination is repeated after the patient has taken galactose, the increase in the rest reduction then found represents the galactose content of the blood.

11. Somogyi: J. Biol. Chem. **75**:33, 1927.

Table 4 shows the results obtained in a number of these experiments in different weeks of the scarlet fever.[12] The fasting values of the rest reduction in scarlet fever appear to be normal. One hour after the ingestion of galactose, the rest reduction, determined in a number of experiments, did not show any change as long as the excretion of galactose was smaller than 0.4 Gm. If the excretion was from 0.4 to 1 Gm., I found small rises in the rest reduction, though not constantly. I never found the combination of an important rise in the rest reduction after the ingestion of galactose and a small excretion of galactose. Therefore the existence of a renal factor could not be

TABLE 4.—*Relation Between the Rest Reduction of the Blood and the Excretion of Galactose in the Urine*

Excretion of Galactose, Gm.	Number Patients	Rest Reduction, Mg. per 100 Cc.
Fasting level	8	22.29
< 0.4	10	Only once > 30 (34)
0.4-0.7	5	41, 21, 38, 48, 44
0.7-1.0	6	22, 35, 27, 46, 60, 33
> 1	6	33, 72, 59, 62, 65, 49

TABLE 5.—*Results of Tolerance Test with 20 Gm. of Dextrose in the Different Weeks of the Illness*

	Greatest Rise in Blood Sugar Content above Fasting Value, per Cent.					
Case	1st Wk.	2d Wk.	3d Wk.	4th Wk.	5th Wk.	6th Wk.
1.....	.....	28.3 (0.127)	38.6 (0.122)	62.36 (0.151)	47.0 (0.131)	47 (0.1295)
2.....	69.4 (0.166)*	39.2 (0.126)	79.5 (0.158)	44.2 (0.137)	34.0 (0.130)	
3.....	35.0 (0.116)	17.6 (0.127)	70.0 (0.132)	65.0 (0.1205)	72.6 (0.145)	
4.....	82.0 (0.132)	36.3 (0.135)	38.0 (0.127)	48.7 (0.116)		
5.....	57.5 (0.156)	64.5 (0.153)	62.0 (0.149)	37.0 (0.131)	71.0 (0.154)	
6.....	21.0 (0.109)	22.5 (0.114)	25.0 (0.110)	30.0 (0.087)	26.5 (0.129)	
7.....	50.0 (0.105)	23.8 (0.104)	29.16 (0.124)	24.5 (0.132)	10.66 (0.109)	
8.....	65.5 (0.139)	65.4 (0.129)	67.8 (0.146)	48.0 (0.117)	20.0 (0.101)	

* Greatest rise in the blood sugar content above the fasting value, 69.4 per cent; highest value, 0.166 per cent.

demonstrated in this way. These experiments further confirm the opinion that the renal threshold for galactose is very low.

A disturbed carbohydrate metabolism caused by disorder in the function of the liver not infrequently manifests itself in an abnormal blood sugar curve after the ingestion of dextrose without the renal threshold for dextrose being exceeded. Such test with dextrose was performed in eight patients during different weeks of their illness; table 5 shows the results of these experiments, each performed with 20 Gm. of dextrose. This table gives the greatest rise in the blood sugar content above the fasting value in per cent and, in parentheses, the highest value itself. The rise in the blood sugar content above the fasting value

12. The observed elevations of the rest reduction are indicated as such and are not expressed in a real percentage of galactose.

might give the impression that in half of the patients the greatest rise was found about the third or fourth week; however, neither the blood sugar curve itself nor the highest value that was reached pointed to the existence of a disturbance in the function of the liver.[13]

The investigation of the function of the liver in scarlet fever had a special significance for me after the observation of sixteen cases of jaundice following scarlet fever. This complication has often been mentioned in the literature [13a] and was also observed earlier in the department of Dr. Herderschee. Clinically this icterus resembled an icterus catarrhalis of short duration. For several days the patients had decolorized feces, dark urine containing bile substances, almost without exception a distinctly enlarged liver and, in the majority of cases, a slightly icteric coloring of the skin and sclerae. The blood serum was icteric to a high degree, and gave a direct and indirect van den Bergh reaction. The time the icterus began in these cases varied, but with one exception it never occurred before the second week of the illness. A small number of the cases occurred at about the same time, giving the impression that there was a small epidemic of icterus.

The idea of some investigators that the icterus is a coincidence [14] and not a real complication of scarlet fever can no longer be accepted generally. In the literature icterus following scarlet fever is mentioned mostly in connection with disease of the liver and bile ducts. Teissier and Duvoir [15] cited Barlow, who observed instances in which death was caused by icterus gravis, and Gouget and Dujarrier, who observed nine cases of extrahepatic diseases of the bile ducts in scarlet fever, e. g., dropsy of the gallbladder, cholecystitis and biliary distention of the gallbladder. According to Jochmann [16] scarlet fever accompanied by obvious icterus with bile substances in the urine and acholic feces is rare. Such icterus in scarlet fever would, according to Popischil, be caused by swelling of the periportal lymph glands. At obduction in a child with scarlet fever, Jochmann once saw dropsy of the gallbladder caused by a large group of glands near the porta hepatis. Recently Schottmüller called attention to the occurrence of hepatitis and cholecystitis as a complication of scarlet fever.[17]

13. We performed one tolerance test with 40 Gm. of dextrose on the twenty-first day of the illness. The blood sugar content rose to 0.157 per cent; no excretion of sugar appeared in the urine.

13a. Recently by Rosenwald, L.: Ueber den Spätikterus bei Scharlach, Ztschr. f. Kinderh. **57**:255, 1931.

14. Rach and von Reusz: Jahrb. f. Kinderh. **76**:422, 1910.

15. Teissier and Duvoir, in Roger, G. E. H.; Widal, F., and Teissier, P. J.: Nouveau traité de médecine et de thérapeutique, Paris, Masson & Cie, 1922, vol. 2, p. 37.

16. Jochmann: Lehrbuch der Infektionskrankheiten für Aerzte und Studierende, ed. 2, Berlin, Julius Springer, 1924, p. 700.

17. Schottmüller: Klin. Wchnschr. **10**:17, 1931. Fahr, T.: Klin. Wchnschr. **10**:20, 1931.

In the children with icterus after scarlet fever I also performed fructose and galactose tests, both during and after the icterus (tables 6 and 7). In the fifteen cases investigated there existed during or after the attack of jaundice decreased tolerance for galactose (in one case

TABLE 6.—*Results of Galactose Test in Fifteen Patients with Icterus After Scarlet Fever*

Case	Day of Illness	Galactose Excreted in Urine after 25 Gm. Was Ingested, Gm.
1	16	2.76
2	12	2.0
3	49	3.52
4	39	2.16
5	40	3.0
6	41	4.93
7	48	3.15
8	14	2.67
9	46	1.95
10	30	4.75
11	17	3.88
12	13	2.16
13	30	2.8
14	12	3.2
15	7	2.86
Average		3.05

TABLE 7.—*Results of Fructose Test (with from 30 to 35 Gm.) in Fifteen Patients with Icterus After Scarlet Fever*

Case	Day of Illness	Fehling Test of Urine After Ingestion of Fructose	Fructose Content of Blood, 1 Hr. After Ingestion, per Cent	Blood Sugar Content, per Cent					Comment
				In Fasting Condition	After ½ Hr.	After 1 Hr.	After 1½ Hr.	After 2 Hr.	
1	18	—	0.004	.....	.....	0.101	.....	.....	
2	11	—	0.008 after ¾ hour	0.092	0.110	0.115	0.102	.....	
3	48	—	0.010 after 1½ hours	.....	.....	.....	.....	.....	
4	40	—	.....	.....	.....	.....	.....	.....	
5	38	—	.....	.....	.....	.....	.....	.....	
6	40	+ (0.07 Gm. sugar)	.....	.....	.....	.....	.....	.....	
7	46	—	.....	.....	.....	.....	.....	.....	
8	15	+ (0.1 Gm. sugar)	.....	.....	.....	.....	.....	.....	
9	47	—	.....	.....	.....	.....	.....	.....	
10	32	—	.....	.....	.....	.....	.....	.....	
11	19	—	.....	.....	.....	.....	.....	.....	
12	14	After reduction	.....	0.071	0.083	0.094	0.082	.....	
13	32	—	.....	0.075	0.077	0.099	0.087	.....	
14	14	—	.....	0.073	0.102	0.094	0.086	.....	
15	8	After reduction	0.008	0.087	0.096	0.094	0.092	0.090	45 Gm. of fructose

in particular); as a rule, the excretion amounted to more than 2.5 Gm. of the ingested 25 Gm., and once to nearly 5 Gm. This corresponds with the result generally obtained in a patient with icterus catarrhalis. In the last mentioned disease tests of the function of the liver with fructose show a distinct disturbance of this function in at least 70 per cent of the cases, also according to my experience. However, in the

fifteen children with icterus after scarlet fever all fructose tests gave negative results (table 7).

This difference between the results of the galactose and the fructose tests in the fifteen children is in agreement with the difference found in a large number of the patients with scarlet fever, especially in the later weeks of the disease. In these cases of icterus the difference manifests itself still more distinctly because the excretion of galactose is so large, and in this way the sensitiveness of both tests is of less importance. Provisionally, I shall here mention only the possibility of a difference between the function of the liver in the icterus occurring after the first stage of scarlet fever and that in icterus catarrhalis.

TABLE 8.—*Protein Spectra of Blood Plasm in Children with Scarlet Fever in the Third and Fourth Weeks of Their Illness*

Case	Week of Illness	Total Protein, per Mille	Albumin, per Mille	Globulin, per Mille	Fibrinogen, per Mille
1	3	66.0	44.8	18.2	3.0
2	3	71.8	45.8	23.4	2.6
3	3	61.8	43.5	14.7	3.6
4	4	61.3	41.8	16.2	3.0
5	4	66.0	42.8	20.6	2.6
6	4	64.7	43.1	18.5	3.1

TABLE 9.—*Results of Fructose Test in a Case of Icterus with Scarlet Fever*

			Blood Sugar Content, per Cent						Urine				
Patient	Day of Illness	Fructose Ingested, Gm	In Fasting Condition	After ½ Hr.	After 1 Hr.	After 1½ Hr.	After 2 Hr.	Fructose Content of Blood, per Cent	Fehling Test	Optical Rotation	Sellwanoff	Bile Substance	Fermentation
W.	12	43	0.153	0.198	0.202	0.194	0.168	.....	Highly +	Inactive	++	++	0.6% sugar
	19	45	0.093	0.118	0.1185	0.120	0.099	0.012	—	Inactive	Slightly +	—	

After the examination of a relatively large number of patients with icterus following scarlet fever had again turned my attention to the function of the liver in the later weeks of the disease, I investigated this function in a small number of cases in another way. In six patients with scarlet fever Dr. W. M. Bendien, of Amsterdam, determined the so-called protein spectrum of the blood plasma, especially in the third and fourth weeks of scarlet fever. No deviations in the function of the liver could be demonstrated. The results of these determinations are given in table 8.

An exception was made of one case of icterus. This case was peculiar, first, because icterus was already present to a high degree at the beginning of the scarlet fever. The patient, an adult, was severelv ill for several weeks. On the twelfth day of his illness a fructose test was performed with 45 Gm.; this showed an enormous increase in

the blood sugar, which was high, in the fasting condition. The urine was strongly reducing and contained dextrose as well as fructose. A week later, when the patient's condition had improved, the fructose test gave negative results. This case may surely be separated from the others.

Finally, among the many cases of scarlet fever investigated I observed only one in which a distinct relapse occurred. Eleven days after the scarlatinal exanthem first appeared in a boy, it reappeared over the whole body, the throat was red, and the urobilin reaction of the urine was strongly positive. In this patient, who showed no jaundice

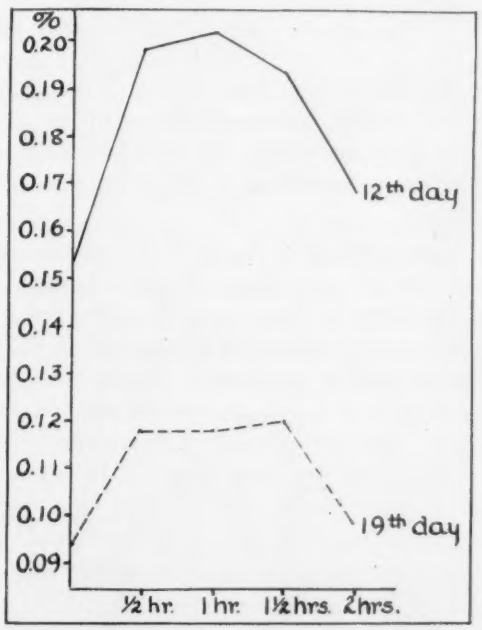


Chart 3.—Blood sugar curve in a case of icterus following scarlet fever (table 9).

and was not very ill at the beginning of his illness, the tolerance for galactose appeared to be severely disturbed; the amount excreted was 4.2 and 4.41 Gm., respectively, on the fourth day of the disease and on the twelfth day after the relapse. Both times, therefore, the excretion was extremely high. The changes in the blood sugar and in the rest reduction of the blood corresponded.

COMMENT

I do not intend to make extensive theoretical comments on the experiments mentioned. I want only to draw attention to the fact

that deviations in metabolism in the later stages of scarlet fever, as revealed in this investigation, have been studied on only a few occasions. Recently Osman [18] and his collaborators found an important fact in relation to acidosis in scarlet fever. The investigation of Koch [19] should also be mentioned. The question whether such changes in metabolism during the later stages of scarlet fever occur accidentally or whether they play some part in creating a predisposition to a complication (nephritis, icterus, etc.) cannot be answered with certainty. The occurrence of these changes perhaps also forms an argument in favor of the conception that a patient with scarlet fever may never be regarded as having recovered before the end of the fourth or fifth week of illness.

SUMMARY

1. In fructose and galactose tests of the function of the liver in a large number of children with scarlet fever during the first days of the illness, only a small percentage of the cases showed slight deviations, which could be demonstrated in the blood and the urine only by means of galactose.

2. With the disappearance of the clinical symptoms of liver insufficiency during the first days of scarlet fever, this disturbance in carbohydrate metabolism could be demonstrated during the following weeks with increasing frequency. The difference between the results of the fructose and galactose tests remained. During the period when the complications of scarlet fever appear, this disturbance of the liver function occurred most frequently, though a direct relation to the involvement of other organs than the liver could not be demonstrated. Tests of the toleration for dextrose for the purpose of judging the changes in the function of the liver did not give definite results.

3. The icterus that frequently occurs in scarlet fever when the first stage is passed clinically resembles icterus catarrhalis. The tolerance for galactose is severely disturbed. In fifteen cases investigated the tolerance for fructose, however, was not distinctly changed. I have mentioned the possibility of a difference between the function of the liver in icterus catarrhalis and that in icterus occurring in scarlet fever after the acute fever stage has passed.

Finally, this investigation deals almost exclusively with mild cases, in accordance with the character of the scarlet fever observed in Amsterdam in recent years.

18. Osman: Guy's Hosp. Rep. **79**:1 (Jan.) 1928.
19. Koch: Ztschr. f. klin. Med. **102**:182, 1926.

TONSILLECTOMY

ITS EFFECT ON THE INCIDENCE, SEVERITY AND COMPLICATIONS OF SCARLET FEVER AND ON THE NUMBER OF HEMOLYTIC STREPTOCOCCI IN THE THROAT

WILLIAM L. BRADFORD, M.D.
ROCHESTER, N. Y.

Since the throat is the site of the primary, if not the most important, lesion in scarlet fever, it is reasonable to suppose that the tonsils play an important rôle in this disease. In this article, an attempt is made to study particularly the effect of tonsillectomy on the incidence, severity and complications and on the occurrence of hemolytic streptococci in the throat during the course of the disease.

In 1930, by actual examination, the incidence of tonsillectomy among 36,038 school children from 5 to 14 years of age was determined.[1] The group represented 52 schools and was a fair sample of the city of Rochester. The percentage of children operated on varied according to the school, the lowest percentage being 19, and the highest 64. The incidence of tonsillectomy also varied with social status, being highest among the well-to-do and the clinic clientele and lowest among the middle class. Finally, it varied according to age as follows:

	per cent
3 — 5 years	10
5 — 6 years	21
7 — 8 years	32
9 —10 years	41
11 —12 years	47
13 —14 years	52

Accurate figures for children under 3 years were not obtainable. From a small sample of preschool children, it was determined that 5 per cent was a fair estimate of the age group "under 5 years."

EFFECT ON THE INCIDENCE

The literature is conflicting concerning the relationship between removal of the tonsils and susceptibility to scarlet fever. Gregory,[2]

From the Department of Pediatrics of the University of Rochester School of Medicine and Dentistry and the Strong Memorial Hospital.

1. Kaiser, A. D.: Personal communication to the author.

2. Gregory, L. T.: Incidence of History of Tonsillectomy in Two Series of Cases of Scarlet Fever: Is Tonsillectomy a Partial Prophylaxis? Illinois M. J. **40**: 210 (Sept.) 1921.

Zikowsky,[3] Jordanoff,[4] Michailovitz[5] and others present evidence supporting the opinion that removal of the tonsils lowers the receptivity for scarlet fever. Cunningham,[6] Kaiser[7] and Stamberger[8] thought that the susceptibility to the disease was little influenced by previous tonsillectomy, while Doull,[9] by a carefully controlled study among children of Baltimore, concluded that the removal of the tonsils has no effect on the incidence of scarlet fever.

FREQUENCY OF SCARLET FEVER AMONG TONSILLECTOMIZED AND NONTONSILLECTOMIZED CHILDREN

In a survey of 48,000 school children in 1927, it was found[10] that among 20,000 in whom the tonsils had been removed, 1,425 (7.6 per cent) gave a history of having had scarlet fever. Among 28,000 children who had not undergone the operation, 4,575 (16 per cent) had the disease. In this survey, it was not determined whether the disease preceded or followed the operation.

In another group in which it was possible to observe the incidence of the disease for a period of ten years, more valuable data were secured.[11] The group consisted of 2,200 children who were tonsillectomized between 5 and 7 years of age and a control group of 2,200 in whose cases operation was advised at the same time but for various reasons was neglected. The incidence of the disease in the two groups is given in table 1.

FREQUENCY OF TONSILLECTOMY AMONG PATIENTS WITH SCARLET FEVER

During a five year period (from July, 1926 to July, 1931), 533 cases of scarlet fever in children were observed at the Rochester Municipal

3. Zikowsky, J.: Tonsillektomie und Scharlach, Wien. klin. Wchnschr. **42**:37 (Jan.) 1929.

4. Jordanoff, K.: Gaumentonsillen und Scharlachinfektion, München. med. Wchnschr. **75**:2172 (Dec.) 1928.

5. Michailovitz, N.: Materialien zum Tonsillarproblem, Zentralbl. f. Hals-, Nasen- u. Ohrenh. **13**:147, 1928-1929.

6. Cunningham, R. L.: Normal, Absent and Pathologic Tonsils in Young Women: A Comparison of Histories, Arch. Int. Med. **47**:513 (April) 1931.

7. Kaiser, A. D.: Incidence of Infection in Tonsillectomized Children, New York State J. Med. **25**:469 (March) 1925.

8. Stamberger, I.: Ueber die Tonsillenfrage auf Grund von 700 Tonsillektomien, Zentralbl. f. Hals-, Nasen- u. Ohrenh. **10**:386, 1927.

9. Doull, J. A.: A Note on the Relationship of Tonsillectomy to the Occurrence of Scarlet Fever and Diphtheria, Pub Health Rep. **39**:1833 (Aug. 1) 1924.

10. Kaiser, A. D.: Incidence of Rheumatism, Chorea and Heart Disease in Tonsillectomized Children, J. A. M. A. **89**:2239 (Dec. 31) 1927.

11. Kaiser, A. D.: The Relation of Tonsils and Adenoids to Infections in Children: Based on a Control Study of Forty-Four Hundred Children Over a Ten Year Period, Am. J. Dis. Child. **41**:568 (March) 1931.

Hospital. In this group, 258 were boys and 275 were girls. The tonsils had previously been removed in 53, or 20.5 per cent, of the boys and in 54, or 19.6 per cent, of the girls.

There were 440 American, 85 Italian and 8 Negro children. Ninety (20.4 per cent) of the American, 17 (20 per cent) of the Italian and none of the Negro children had previously been tonsillectomized.

The distribution of the cases according to schools, social status and the like, was such that they represented a fair sample of the children of Rochester. The expected percentage of tonsillectomies as determined in 1930 was therefore considered sufficiently accurate to be applicable in this study.

TABLE 1.—*Frequency of Scarlet Fever Among Tonsillectomized and Non-tonsillectomized Groups of Children*

		Incidence of Scarlet Fever		
	Number of Cases	Before 6 Years (Age of Operation)	During Next 10 Years	Total Incidence 6–16 Years, Per Cent
Tonsils removed	2,200	198 (9%)	73 (3.3%)	12.3
Removal advised, but declined	2,200	242 (11%)	102 (4.6%)	15.6

The group of 600 cases in which the incidence of tonsillectomy was studied consists of the 533 hospital cases and 67 cases seen in private practice during 1931. The relationship of tonsillectomy in this group of patients with scarlet fever is represented in table 2:

TABLE 2.—*A Comparison of the Actual with the Expected Rate of Tonsillectomy Among Six Hundred Cases of Scarlet Fever*

	Total Number of Cases	Percentage of Rochester Children with Tonsils Out	Expected Number of Children with Scarlet Fever with Tonsils Removed	Actual Number of Children with Scarlet Fever with Tonsils Removed
Under 5 years	195	5	9.7	12
5– 6 years	128	21	26.8	17
7– 9 years	121	32	38.7	34
9–10 years	77	41	31.5	25
11–12 years	57	47	26.7	21
13–14 years	22	52	11.4	13
Total	600		144.8 (24%)	122 (20%)

It is evident from table 2 that the difference (4 per cent) between the percentage actually operated on and the expected percentage operated on in such a sample is statistically insignificant;[12] i. e., the difference in percentages is less than 3 times the standard error of difference.

12. The formula used was:

$$\text{Standard error of difference} = \sqrt{\frac{(\%\text{ of A})\,(100 - \%\text{ of A})}{\text{Number of A}} + \frac{(\%\text{ of B})\,(100 - \%\text{ of B})}{\text{Number of B}}}$$

Considering, therefore, both the frequency of scarlet fever in tonsillectomized and nontonsillectomized groups of children and the frequency of tonsillectomy among cases of scarlet fever, it seems that there is a slight, though insignificant, beneficial effect of removal on susceptibility to scarlet fever. It is significant that a similar conclusion was reached by Doull [9] in a well controlled study of the subject among the children of Baltimore.

EFFECT ON THE SEVERITY OF THE DISEASE

Information concerning the effect of previous removal of the tonsils on the severity of a subsequent attack of scarlet fever is fragmentary, and consists chiefly of clinical impression. Kaiser,[10] in a study of 1,200 tonsillectomized children, concluded that the operation somewhat lessened the severity of the disease. Place [13] thought that removal early in the course of the infection reduced the danger of complications. Bullowa [14] found that 16 of 154 patients had previously undergone

TABLE 3.—*Distribution in Five Hundred and Thirty-Three Cases*

	Tonsils In	Tonsils Out
Mild	166 (38.9%)	46 (43%)
Moderately severe	175 (41.0%)	46 (43%)
Severe	85 (18.9%)	15 (14%)
Total	426	107

tonsillectomy. Eleven of the cases were mild and 5 were moderately severe. The patients all seemed to have less adenitis and less severe rashes. He thought that prophylactic removal prevented some of the severe complications.

In a group of 533 hospital cases concerning which accurate records were kept, the distribution according to the degree of severity was as shown in table 3.

In this group, there is little evidence that previous tonsillectomy influenced the initial severity of the infection.

EFFECT ON THE DEVELOPMENT OF COMPLICATIONS

In the same group of children, data concerning the development of complications were available. Table 4 presents the incidence of various complications as observed among the tonsillectomized and the non-tonsillectomized group.

13. Place, E. H.: Tonsillectomy in Contagious Diseases, Boston M. & S. J. **187**:434 (Sept. 21) 1922.

14. Bullowa, J. G. M.: The Tonsils and Scarlet Fever, Am. J. Dis. Child. **22**:29 (July) 1921.

From the foregoing data, it is difficult to conceive that the tonsillectomized group in general enjoyed more protection than the nontonsillectomized group so far as complications are concerned.

EFFECT ON THE PERCENTAGE OF HEMOLYTIC STREPTOCOCCI IN THE THROAT IN SCARLET FEVER

Among normal persons, the percentage harboring hemolytic streptococci in their throats has been reported as varying from 5 to 90 (Tongs,[15] Pilot and Davis,[16] Opie and his co-workers,[17] Smillie,[18] Ruediger,[19] Toyoda and his co-workers [20] and others). Among tonsillectomized children, it has ranged from 5 to 23 (Tongs,[15] Pilot and Davis,[16] Simmons and Taylor,[21] Nichols and Bryan [22] and Van Dyke.[23]

TABLE 4.—*Relationship of Tonsillectomy to the Occurrence of Complications of Scarlet Fever*

	Tonsils In	Tonsils Out
Total number of cases	426	107
Number developing complications	200 (46.9%)	47 (43.9%)
Otitis media	117 (27.4%)	27 (25.2%)
Mastoiditis	40 (9.1%)	13 (12.1%)
Sinusitis	14 (3.2%)	5 (4.7%)
Cervical adenitis	40 (9.1%)	12 (11.2%)
Pulmonary disease	20 (4.7%)	3 (2.8%)
Cardiac disease	7 (1.6%)	5 (4.7%)
Nephritis	18 (4.2%)	6 (5.6%)
Pyuria	9 (2.1%)	1 (0.9%)
Abscess (paronychia, etc.)	22 (5.1%)	4 (3.7%)
Arthritis	8 (1.8%)	3 (2.8%)
Sepsis	6 (1.4%)	3 (2.8%)
Death	8 (1.8%)	5 (4.7%)

15. Tongs, M. S.: Hemolytic Streptococci in the Nose and Throat: With Special Reference to Their Occurrence After Tonsillectomy, J. A. M. A. **73**:1050 (Oct. 4) 1919.

16. Pilot, I., and Davis, D. J.: Hemolytic Streptococci in the Faucial Tonsil and Their Significance as Secondary Invaders, J. Infect. Dis. **24**:386, 1919.

17. Opie, E. L.; Freeman, A. W.; Blake, F. G.; Small, J. C., and Rivers, T. M.: Pneumonia at Camp Funston, J. A. M. A. **72**:108 (Jan. 11) 1919.

18. Smillie, W. G.: Studies of the Beta Hemolytic Streptococcus (Smillie and Brown), J. Infect. Dis. **20**:45, 1917.

19. Ruediger, G. F.: The Streptococci from Scarlatinal and Normal Throats and from Other Sources, J. Infect. Dis. **3**:755, 1906.

20. Toyoda, T.; Kuivi, C.; Moriwaki, J., and Futagi, Y.: Is the Haemolytic Streptococcus Acceptable Epidemiologically as the Aetiological Agent of Scarlet Fever? Brit. J. Child. Dis. **28**:89 (April-June) 1931.

21. Simmons, J. S., and Taylor, R. E.: Bacterial Carriers in the Upper Respiratory Tract, J. A. M. A. **72**:1885 (June 28) 1919.

22. Nichols, H. J., and Bryan, J. H.: The Tonsils as Foci of Infection in Streptococcus Hemolyticus Carriers, J. A. M. A. **71**:1813 (Nov. 30) 1918.

23. Van Dyke, H. B.: Hemolytic Streptococci in the Normal Throat After Tonsillectomy, J. A. M. A. **74**:448 (Feb. 14) 1920.

In children, the incidence and number of hemolytic streptococci in the nasopharynx are decidedly less after adenotonsillectomy, but removal does not entirely cause their disappearance.[24] In the cases of carriers of Streptococcus epidemicus, tonsillectomy causes complete and rapid disappearance of the organisms from the throat.[25]

It would therefore seem that previous removal of the tonsils would lead to the occurrence of fewer numbers of hemolytic streptococci in the throats of children in whom scarlet fever later develops.

During a three year period (from 1928 to 1931), routine cultures for hemolytic streptococci were carried out on specimens from the throats of all patients with scarlet fever admitted to the pediatric contagious service of the Rochester Municipal Hospital.

The technic was as follows: The patient was forced to gag, and each tonsillar surface and the pharynx were swabbed. Ten cubic centimeters of Douglas broth was immediately innoculated with the swab. Dilutions were made from this, and blood-agar plates were then

TABLE 5.—*The Relationship of the Number of Organisms in the Throat at the Onset of the Rash to the Presence or Absence of Tonsils*

		Percentage of Hemolytic Streptococci in the Throat						
	Cases	None	-5	5-25	30-50	55-75	80-100	Average
Tonsils in.....	312	27	89	75	59	34	28	26.7
Tonsils out.....	85	9	33	19	13	7	4	21.0

poured from each dilution. After from twenty-four to forty-eight hours, the plates were read, and the percentage of hemolytic colonies characteristic of the hemolytic streptococcus was determined by count.

It is interesting to note the relationship between the percentage of hemolytic streptococci in the first culture (within forty-eight hours of the onset of the rash) and the presence or absence of tonsils.

From the results in table 5, there is apparently, as an average, a slightly lower percentage of hemolytic streptococci in the throats of children without tonsils during the first days of infection.

A similar slight difference in favor of the tonsillectomized child is apparent when the degree of severity of the disease is correlated with the percentage of streptococci in the throat. Table 6 represents such a comparison.

24. Meyer, J.; Pilot, I., and Pearlson, S. J.: Bacteriologic Studies of the Upper Respiratory Passages: IV. Incidence of Pneumococci, Hemolytic Streptococci, and Influenza Bacilli (Pfeiffer) in the Nasopharynx of Tonsillectomized and Non-Tonsillectomized Children J. Infect. Dis. **29**:59 (July) 1921.

25. Pilot, I., and Davis, D. J.: Tonsillectomy in Carriers of Streptococcus Epidemicus, J. Infect. Dis. **48**:501 (May) 1931.

Thus, it is seen that there is a slight increase in the number of organisms according to the severity of the disease in the tonsillectomized group as well as in the group not operated on.

Is the child with more streptococci in his throat more likely to develop complications? This question is answered by the data in table 7.

TABLE 6.—*The Relationship of the Number of Organisms in the Throat to the Severity of the Disease*

	Mild	Moderately Severe	Severe
Tonsils in: number of cases	132	115	61
Average percentage of hemolytic streptococci in throat	21.6	28.0	38.0
Tonsils out: number of cases	40	35	13
Average percentage of hemolytic streptococci in throat	16.1	27.6	25.5

TABLE 7.—*The Relationship of the Number of Organisms in the Throat (Original Culture) to the Occurrence of Complications*

		Number of Cases	Average Percentage of Hemolytic Streptococci in the Throat (First Culture)
Tonsils in:	No complications	157	25.3
	Had complications	151	26.4
Tonsils out:	No complications	49	18.9
	Had complications	40	18.6

TABLE 8.—*Comparison of the Rate of Disappearance of the Organisms from the Throat in Tonsillectomized and Nontonsillectomized Children*

		1–10 Days		11–20 Days		21–30 Days		Total	
	Number of Cases	Number of Cultures	Average Percentage of Streptococci	Number of Cultures	Average Percentage of Streptococci	Number of Cultures	Average Percentage of Streptococci	Number of Cultures	Average Percentage of Streptococci
Tonsils in:									
No complications	141	164	23.6	61	9.7	159	7.1	384	14.7
Complications	149	153	29.1	71	12.4	135	11.3	359	19.1
Tonsils out:									
No complications	48	59	16.9	22	7.3	36	6.8	117	12.0
Complications	39	39	18.4	26	15.2	21	10.9	86	15.3

In either group, the percentage of organisms in the original culture is practically the same regardless of whether later complications develop.

THE DISAPPEARANCE OF HEMOLYTIC STREPTOCOCCI DURING SCARLET FEVER

In 290 children with tonsils and in 87 without them, the average percentage of hemolytic streptococci was determined by ten day periods during the first thirty days after the appearance of the rash. The results are expressed in table 8.

It is apparent from tables that there is little difference in the rate of disappearance of the organism from the throat in the tonsillectomized and in the nontonsillectomized child. In either group, however, there is always a slightly higher percentage of organisms in the throats of those in whom complications develop.

Considering further the number of children in each group who at the end of thirty days possessed excessive numbers of hemolytic streptococci in their throats, 64 (22 per cent) of the 290 children with tonsils and 15 (17.2 per cent) of the 87 without tonsils possessed organisms in the throat in excess of 5 per cent. In each group, about one-half had complications at that time.

Carriers, therefore, are about as frequent at the end of the usual thirty day period of isolation among tonsillectomized children as among those who retain their tonsils.

SUMMARY

In a group of 600 patients with scarlet fever, 122 (20 per cent) had previously been tonsillectomized. The expected number operated on for the community from which the sample was secured should have been 144 (24 per cent). Therefore, a slight but statistically insignificant beneficial effect of tonsillectomy on the incidence of the disease occurred.

The degree of severity of the disease was about the same in the tonsillectomized and in the nontonsillectomized children, in a series of 533 hospital cases.

Forty-seven (43.9 per cent) of the tonsillectomized group and 200 (46.9 per cent) of the nontonsillectomized group developed complications.

At the appearance of the rash, the average percentage of hemolytic streptococci in the throats of 312 children with their tonsils in was 26.7. In a group of 85 without tonsils, it was 21.0.

In either group, the percentage of streptococci increased slightly with the degree of severity of the disease.

The average percentage of streptococci in the throat during the first few days of scarlet fever were about equal in the children who later developed complications and in those who escaped. This was true regardless of whether or not the child had previously been operated on.

The rate of disappearance of the organism from the throat was about equal in children with and in those without tonsils. The tonsillectomized child, however, had a few less organisms throughout convalescence.

At the end of the usual period of isolation of thirty days, 17 per cent of the tonsillectomized group and 22 per cent of the nontonsillectomized group had hemolytic streptococci in their throats in excess of 5 per cent.

A SYNDROME OCCURRING IN THE NEONATAL PERIOD MANIFESTING TETANY-LIKE SYMPTOMS

HAROLD T. NESBIT, M.D.
DALLAS, TEXAS

Some controversy exists as to the presence of tetany in the neonatal period. Grulee [1] stated that "whether such a condition may be found during the first few weeks of life is doubtful." At the Dallas Southern Clinical Society, on April 1, 1931, he stated that he had never observed an instance of tetany during the first six weeks of life. Other excellent observers, notably von Reuss,[2] believe that tetany does not occur during the new-born period. Pediatric textbooks fail entirely to mention this condition as being present at this interval of life. Kehrer [3] described six instances of a syndrome that he believed to be tetany. Shannon [4] has recently presented nine additional instances, described as tetany, occurring in infants less than 1 week of age. Grulee, on reviewing the groups of cases of Kehrer and Shannon, believed that certain clinical features were present that made a diagnosis of tetany improbable.

There are certain characteristics of this condition that do warrant special consideration, i. e., the edema and cyanotic spells described by Kehrer and Shannon, as well as the character of the stridor, which are illustrated in the cases herewith presented. In many other respects the symptoms associated do not differ from tetany occurring in other periods of life.

To discuss the question as to whether this entity should be designated tetany or whether it is an entirely different syndrome is not the purpose of this presentation. However, to support the contention that this rather classic condition occurs in the neonatal period and to illustrate its characteristics further, the following cases are presented.

From the Department of Pediatrics, Baylor University.

Read before the Dallas Pediatric Society, April 4, 1931.

1. Grulee, C. G.: Clinical Pediatrics, New York, D. Appleton and Company, 1926, vol. 3, p. 246.

2. von Reuss, A. R.: Diseases of the New-Born, New York, William Wood & Company, 1922, p. 343.

3. Kehrer, E.: The Obstetrical and Gynecological Significance of Tetany, Arch. f. Gynäk. **99**:372, 1913.

4. Shannon, W. R.: Tetany, Generalized Edema and Cerebral Compression in the New-Born, Arch. Pediat. **48**:153 (March) 1931.

REPORT OF CASES

CASE 1.—B. B. D., whose delivery on Aug. 18, 1930, was normal, at birth weighed 7 pounds and 10 ounces (3,400 Gm.). The mother had one miscarriage two and one-half years previously. The family history otherwise was negative. During the first four days after birth the infant had a good lusty cry. It was breast fed and received dextrose solution as a complementary feeding, which it retained. The infant was very nervous and cried continually. Slight jarring of the bed caused an attack during which the head was retracted and all four extremities were thrown into spasm. Slight cyanosis accompanied these attacks. On the fifth day the stools became frequent, green and watery. The buttocks were excoriated. At this time two teaspoonfuls of castor oil were given. During the following six days, the character of the stools remained unchanged. The infant was placed at the breast, but was indifferent to nursing. On the tenth day when the child was seen by me in consultation he presented the following picture:

The infant's weight had fallen to 6 pounds and 15 ounces (3,100 Gm.). It was vomiting the breast milk. The stools were of the character described. General rigidity was present over the body. The hands were clinched in fist position. The arms remained flexed at the elbows. The feet were extended at the ankles. The toes were flexed, and the legs were flexed at the knees. Passive resistance of the extremities was present, owing to hypertonia. The head was held slightly retracted. The infant fretted continually, but could not cry aloud, although grimaces were made. A slight jarring provoked a spasm, indicated by extension and clonic contracture of all the extremities. During these spasms the head became retracted. At times a spasmodic strabismus was noted during these spells. Between attacks the body assumed the position described. The Chvostek sign was present, causing a jerking of the masseter and muscles of the neck in addition to contraction of the lips and inner canthus of the eye. The knee and achilles jerks were very active. Trousseau's phenomena could not be elicited, because of the presence of continual spasm. Ankle clonus was present. The infant perspired freely. The dorsa of the feet were edematous, as indicated by pitting. Determination of the blood calcium was made, which proved to be 8 mg. per hundred cubic centimeters of blood. The Wassermann reaction of the blood was negative.

The infant was given protein milk, 1 ounce, and then was allowed to nurse. Calcium gluconate, 10 grains (0.65 Gm.), was given orally every three hours. Collip's parathyroid, 5 units, was given subcutaneously. This procedure was repeated the next day. During the following two days the weight fell to 6 pounds and 13 ounces (2,900 Gm.), probably from the loss of fluid, the edema of the ankles having disappeared during the interim. The baby no longer fretted. A high-pitched cry was noted. The calcium gluconate was continued, and by the end of four days all symptoms of tetany had disappeared. Determination of the blood calcium at this time showed 10.2 mg. per hundred cubic centimeters. A gain of 7 ounces (0.09 Kg.) occurred during the subsequent week.

The infant was dismissed from Baylor Hospital on September 3. During the following month, the administration of 35 grains (2.28 Gm.) of calcium gluconate was continued daily. After the drug was discontinued, fretfulness and hyperexcitability were noted. On the administration of calcium for a period of one month these symptoms entirely disappeared. During the intervening four months the child has received viosterol in addition to cereals and vegetables. No symptoms of tetany are now present. The infant appears to be normal in every respect.

CASE 2.—B. G. T., born on Nov. 24, 1930, a first-born child, weighed 7 pounds and 12½ ounces (3,500 Gm.) at birth. Labor was difficult, requiring the use of high forceps. The infant was revived with difficulty, and during the first two days

had repeated cyanotic spells, associated with irregular respiration, and spasms involving the left upper and lower extremities. The child was unable to cry aloud. Alpha lobeline, oxygen and carbon dioxide had been administered after each spell. The condition apparently became worse, the child being seen by me in consultation on November 26. At this time the infant had been fed on a formula of Dryco, which it vomited immediately after taking. The weight had fallen to 7 pounds and 3 ounces (3,290 Gm.). Almost continual tremor of the left arm and leg was noted. Between attacks the hands would assume a fist position. The feet were extended at the ankles. The toes flexed; the arms also flexed at the elbows. All extremities were very hypertonic. During the cyanotic spells, which were easily provoked by a loud noise or jarring, the eyes would go into a concomitant strabismus. The Chvostek sign was present, including jerking of the inner canthus of the eyes, the lips and the muscles of the neck. Traction of the head would occur during the spells, but it would relax completely during the intervals between the attacks. The cry was barely audible, and was of a high-pitched character. Edema of the dorsa of the feet was noted. Ten cubic centimeters of whole blood was given intramuscularly, and fibrinogen, one-half ampule, was given every three hours, the condition then being considered the result of a cerebral hemorrhage following the severe labor or due to a tendency to bleed. The bleeding time proved to be three and one-half minutes, and the blood calcium 9 mg. per hundred cubic centimeters. On November 27, the administration of fibrinogen was stopped. Calcium gluconate, 40 grains (2.6 Gm.), was given in the formula daily. Within forty-eight hours the cyanotic spells had lessened. The tremor, however, now included all of the extremities. During the following four days the edema disappeared, and the hypertonicity and hyperexcitability lessened. The child was placed at the breast and nursed well. On December 2, the weight was 7 pounds and 10½ ounces. No further spasms or cyanotic spells were present. The extremities became relaxed. The infant did not go into spasm as it formerly had when the crib was jarred. The cry was normal. The administration of calcium was stopped. The blood calcium at this time was 10 mg. per hundred cubic centimeters.

The infant was seen on March 25, 1931, at the age of 4 months. The weight was 14 pounds and 14 ounces (6,770 Gm.). One teaspoonful of cod liver oil has been given three times a day in addition to 1 ounce (29.57 cc.) of tomato juice. Complementary feedings have been unnecessary. No further symptoms of tetany have been noted.

Case 3.—B. B. E., aged 11 days, was seen on Jan. 10, 1931. The mother had had one stillbirth two and one-half years previously; otherwise the family history was unimportant. The birth weight was 9 pounds and 7 ounces (4,290 Gm.). Labor was normal. The child was seen by me in consultation because it had fretted and vomited continually since birth. Although the mother had an abundance of milk, the child's weight had fallen to 8 pounds (3,600 Gm.). Following nursing, projectile vomiting had occurred. The stools were normal. The mother complained that the child had blue spells. An enlarged thymus had been considered by the attending doctor. The infant was hypertonic and fretted almost continually, the cry being high-pitched. Spasm of the extremities associated with cyanosis and retraction of the head was easily elicited by the jarring of the cradle. When not in spasm the hands remained in a fist position, the elbows flexed. The legs were flexed at the knees, the feet were extended, and the toes were flexed. Elicitation of the Chvostek sign caused a pursing of the lips. The infant was given atropine sulphate, 1 drop of 1:1,000 solution, subsequently increased to 3 drops, preceding each nursing. Later, thick cereal, 2 drachms, were necessary

before each feeding to prevent vomiting. A roentgenogram of the chest was made, the report indicating a slight enlargement of the thymus. Determination of the blood calcium revealed 9 mg. per hundred cubic centimeters. The Wassermann reaction of the blood was negative. No treatment was given for the enlarged thymus. The hypertonicity, fretting, spasm and cyanotic spells persisted. Calcium gluconate, 7½ grains (0.49 Gm.), orally every three hours, was prescribed. On January 29 the vomiting responded to the administration of thick cereal and atropine. On this date the infant presented the following symptoms:

It fretted almost continuously, although it retained its formula well and had gained so that it weighed 9 pounds and 15 ounces (4,507 Gm.). According to the mother, the blue spells occurred whenever the baby was disturbed. Accompanying the blue spells, the child would have a spasm of the extremities as previously described. It was learned at that time that the mother was giving the child only 7½ grains of calcium, daily, instead of every three hours. During the following six weeks, the child received calcium gluconate, 60 grains (3.9 Gm.), daily.

When seen on March 12, the baby was not hypertonic. The mother said that the blue spells accompanied by the retraction of the head and spasm of the extremities had completely stopped. The infant no longer wakened with a start when a door was closed. The cry was lusty. The child appeared to be normal in every respect. The weight was 11 pounds and 6½ ounces (5,189 Gm.). The calcium was discontinued, and viosterol, 16 drops, was given instead. The serum calcium was 10.5 mg. per hundred cubic centimeters.

Case 4.—B. B. B., born on Feb. 24, 1931, was a first-born child. Delivery was difficult, and the birth weight was 9 pounds and 13½ ounces (4,400 Gm.). During the first two days the infant had repeated spells of cyanosis, necessitating oxygen and the administration of carbon dioxide. With each attack the head became retracted, and spasmodic strabismus was noted, in addition to spasm of all the extremities. The child was seen by me on February 26 in consultation. The condition had been considered the result of cerebral injury resulting from trauma at the time of birth. The bleeding time was three and one-half minutes. Ten cubic centimeters of whole blood from the father had been given intramuscularly. The child presented the following clinical symptoms:

General hypertonicity was present. The position of the extremities was that described in the preceding cases. Tapping of the cheek caused a pursing of the lips, accompanied by a protrusion of the tongue. Ankle clonus was present. The knee jerks were exaggerated. Jarring of the bed would inaugurate a cyanotic attack, accompanied by an extension of the arms and legs and a fibrillary tremor. At rest the hands became clinched, the feet were extended at the ankles, the toes were in plantar flexion and the legs and arms were partially flexed at the knees and elbows. The infant was unable to cry aloud. The spells of cyanosis occurred at intervals of about one hour. Attempts to get blood for determination of the blood calcium were unsuccessful. The bleeding time was normal. A roentgenogram of the chest revealed no atelectasis; there was no enlargement of the thymus. Spinal puncture revealed no blood cells, although the pressure was increased. The weight had fallen during the two days to 9 pounds (4,100 Gm.).

Because of gratifying results following its use in a similar case, Collip's parathyroid, 5 units, was given subcutaneously. Calcium gluconate, 10 grains, was added to the formula every three hours. On February 27 the cyanotic spells had completely stopped; otherwise the condition of the infant remained unchanged. Parathyroid, 5 units, was again administered. Calcium gluconate in the amounts stated was given in the formula. The cry on February 28 became high pitched, gradually assuming a normal character before the infant's departure from the

hospital. On the day of dismissal from the hospital no hypertonia was present. The child was discharged on March 3, at which time spasm of the extremities could not be elicited. The weight had increased to 9 pounds and 5 ounces (4,220 Gm.). At the time of writing the infant is more than a month old, and is making normal progress.

CASE 5.—B. G. T., born on March 1, 1931, was a first-born infant. The birth weight was 7 pounds and 8 ounces (3,400 Gm.). The family history was unimportant. Labor was prolonged, forceps being required for delivery. Great difficulty was experienced by the obstetrician in reviving the infant at birth. During the first day, the child had repeated cyanotic spells and spasms, elicited by jarring the bed. The infant was hypertonic, being unable to cry aloud. The spells of cyanosis and tremor of all the extremities, accompanied by retraction of the head, occurred frequently, and could even be inaugurated by noise in the nursery. The infant resembled in nearly every way those previously described, with hands clinched, pedal spasm and a positive Chvostek sign. The bleeding time was three and one-half minutes. Spinal puncture revealed increased pressure. No red blood cells were present in the spinal fluid. The blood calcium was 10.4 mg. per hundred cubic centimeters. Ten cubic centimeters of whole blood from the father was given intramuscularly. Collip's parathyroid extract, 5 units, subcutaneously, and calcium gluconate, 10 grains, orally every three hours, were given on March 2. On March 3 the administration of parathyroid was repeated. The administration of calcium was continued during the infant's stay in the hospital. During this period the cry became high-pitched, later becoming entirely normal. On March 6, the final day in the hospital, no further spells of cyanosis or spasm were present, nor could they be elicited by jarring the bed. The weight, which had fallen to 6 pounds and 15 ounces (3,180 Gm.), increased to 7 pounds and 1 ounce (3,240 Gm.). On the day of departure the child was completely relaxed. Since returning home the infant has continued to make good progress. Viosterol has been given daily. The calcium has been stopped.

CASE 6.—B. B. R., a boy, born on March 4, 1931, was a first-born child. The mother was in labor fourteen hours, and the child was delivered by low forceps. The delivery was not difficult. Following delivery the child remained cyanotic for fifteen minutes. Alpha lobeline was administered. The respirations came in gasps only. During the first day cyanotic spells were frequent. During these attacks the respirations would become irregular. The lobeline appeared to give some relief. The infant could not cry aloud, although he fretted continually and made grimaces in his effort to cry. Twelve hours after birth the dusky cyanosis became worse with each spell. Twitching of the right arm was almost continuous. Attacks beginning with cyanosis, retraction of the head accompanied by a tremor of the right upper extremity and finally including the other extremities, occurred at frequent intervals. The Chvostek sign was slightly active. On March 5, fourteen hours after delivery, 7 cc. of blood from the father was given intramuscularly. Calcium gluconate, 35 grains (2.28 Gm.) was given daily in the formula. No improvement was noted on the following day. The infant was fed a formula of Dryco with a Breck feeder. The ensuing week a gradual amelioration of the clinical symptoms enumerated was witnessed. On March 9 the cry was audible for the first time, being high-pitched. On March 10 the spells of cyanosis, accompanied by retraction of the head, were no longer in evidence. The cry was normal. Jarring of the crib produced a tremor of the right upper extremity only. Tapping of the facial nerve produced no contraction. The infant now nursed satisfactorily, although complementary feedings of Dryco were necessary. Two days later the

tremor of the right upper extremity no longer could be produced. Continued administration of calcium gluconate and the administration of viosterol was prescribed, the patient being dismissed from the hospital on March 12.

Although this patient has not been seen during the intervening weeks, a report from the attending physician indicates that the baby is fretful, that minor disturbances will inaugurate a tremor of all the extremities, but that no cyanotic spells have occurred. Viosterol and calcium have not been administered.

COMMENT

In summary, the six cases present almost identical symptoms, those of a hypertonic infant with spastic contractures of the upper and lower extremities, a positive Chvostek sign and hyperactive reflexes. In cases 3, 4 and 5, clonic contractions of all the extremities were precipitated by the slightest disturbance, such as jarring the bed. In case 2 this spasm was noted first in the upper and lower left extremities. Later, however, all the extremities were included. In case 6 the spasm was first noted in the right arm. During these spasms the head became retracted, and in cases 1 and 2 a concomitant strabismus occurred simultaneously. When not in spasm the hands assumed a fist position, the feet were extended at the ankles, flexion of the toes was present, and the elbows were flexed. Trousseau's phenomena could not be elicited, because of the continued flexure caused by the hypertonicity. The lack of proper equipment forestalled the appliance of Erb's sign.

These symptoms coincide with those presented by Kehrer and Shannon in describing tetany of the new-born.

Among the symptoms which require special mention are the following: The character of the cry was a striking symptom in these six infants. Typical laryngospasm has not been described during the first few weeks of life. In Shannon's series a peculiar cry, somewhat resembling a cephalic cry, of high-pitched character, was noted. The inability of four of the infants in the present group to cry aloud was a striking symptom. In cases 2 and 3 the cry was high-pitched. Following the administration of calcium and parathyroid extract the cry in each instance gradually assumed a normal character, and amelioration of the other clinical symptoms occurred. It is indeed plausible that the spasm generally present thoroughout the body musculature could include spasm of the laryngeal musculature. The prompt relief from this symptom following the use of calcium therapy indicates that a deficiency of this element is a responsible factor.

The edema and cyanosis seen in these cases have also been noted previously.[5] The association of edema with a decreased calcium concentration and the further knowledge that a lowered availability of

5. Kehrer (footnote 3). Shannon (footnote 4). Shannon, W. R.: A Case of Tetany and Edema in the New-Born, Minnesota Med. **13**:476 (July) 1930.

serum calcium is a factor accompanying tetanic manifestations must indicate the common origin of these phenomena. The rapid improvement of the edema, cyanosis and tetany after the administration of calcium and parathyroid, it seems, should establish this fact. The knowledge concerning the rôle of calcium in preservation of the normal water balance of the body is of an indirect nature, having been gained from investigations of the effect of this element in experimental and clinical edema. It is apparent, however, that calcium and other inorganic elements are of the greatest importance in maintaining the normal water balance. Calcium presumably exerts its effect on the permeability of the capillaries or on the hydration capacity of the colloids, which properties are probably dependent on its stabilizing effect on the colloidal system. Normal permeability depends to a great extent on the presence of a normal balance between the inorganic ions, calcium, sodium and potassium, decrease in calcium resulting in an increased permeability. Osterhout [6] suggests that sodium and calcium combine with some constituents of the cell, and that the permeability of the cell membrane varies according to the relative proportions in which these two combinations of the cell constitutents are present. Cantarow [7] remarked that "It seems strange that marked diminution in serum calcium, such as occurs in tetany of parathyroid origin, is not accompanied by profound disturbance of the water balance of the body. The occasional puffiness of the skin, localized edema and intermittent hydrarthrosis, which occur in acute and chronic parathyroid insufficiency, may be an evidence of this disturbance." Falta [8] describes edema of the hands and feet as a common finding in tetany. Feer [9] has noted generalized edema associated with tetany. Shannon [4] has called attention to the association of cyanosis with edema of the subcutaneous tissue and tetany in new-born infants. He is of the opinion that the cyanotic spells are due to edema of the brain, resulting from a calcium disturbance. He administered calcium and parathyroid extract, causing a cessation of the attacks of cyanosis which, in some instances, were severe enough to endanger greatly the infant's life. One patient of his group died one hour after the first examination. Autopsy proved that death was due to cerebral edema—no hemorrhage was present. Had more than an hour been permitted for the body's utilization of the parathyroid extract which was administered, he believes that the infant might have recovered.

---

6. Osterhout, W. J. V.: Antagonism and Permeability, Science **45**:97, 1917.

7. Cantarow, Abraham: Calcium Metabolism and Calcium Therapy, Philadelphia, Lea & Febiger, 1931.

8. Falta, W., and Kahn, S.: Tetany of the Viscera, Med. Klin. **7**:1775 (Nov. 12) 1911.

9. Feer, E.: Diseases of Children, Philadelphia, J. B. Lippincott Company, 1928, p. 58.

In cases 3 and 6, in which no parathyroid was given, calcium alone being used, the improvement that resulted was less prompt. From this it is evident that administration of parathyroid will bring quicker relief by making calcium immediately available, possibly by alteration of the calcium ions of the plasma or by skeletal depletion.

The serum calcium of 8, 9, 9 and 10.4 mg. per hundred cubic centimeters in cases 1, 2, 3 and 5, respectively, deserves mention, since pediatric texts as well as such observers as Howland and Marriott,[10] Kramer, Tisdall and Howland,[11] describe the normal level as lying between 9 and 11 mg. per hundred cubic centimeters. It is a common belief that only when serum calcium is reduced to about 7 mg. per hundred cubic centimeters will typical spells of tetany appear. More recent studies of Jones [12] revealed that the plasma calcium in twenty-two infants from 4 hours to 12 days old averaged 12.3 mg.; Mayer [13] found that the average serum calcium in children from 4 to 11 years was 11.38 mg.; Nohlen [14] found 12.65 mg. in new-born infants, and Leicher,[15] 11.6 mg. during the first and second decades, gradually decreasing to 10.8 mg. at 50 years of age or over. From this it appears that serum calcium during infancy is above that present during adult life. It is easy to conceive then that a serum calcium of 10 or 11 mg. in a new-born infant can be considered as being below the normal level. Shannon has described tetany occurring in an infant in whom the serum calcium was 10 mg. In case 5, in which the serum calcium was 10.4 mg., typical symptoms of tetany occurred. The finding of a calcium level of 8 and 9 mg. in cases 1 and 2, respectively, together with the higher levels of 10 and 10.2 mg. following the administration of parathyroid and calcium, indicating that the level of the total blood calcium is an etiologic factor, bears some consideration. In juveniles and adults symptoms of tetany may be absent in some cases when the serum calcium is 7 mg. per hundred cubic centimeters and present in others when it is at a higher level. It is likely, however, that the factor that determines the development of tetanic manifestations in the new-born infant probably is not

---

10. Howland, J., and Marriott, W. McK.: Calcium Content of Blood in Infantile Tetany, Quart. J. Med. **11**:289 (July) 1918.

11. Kramer, B.; Tisdall, F. F., and Howland, J.: Clinical Significance of Calcium Concentration in Serum of Children and Possible Errors in Its Determination, Am. J. Dis. Child. **22**:560 (Dec.) 1921.

12. Jones, M. R.: The Calcium Content of Blood Plasma and Corpuscles in the New-Born, J. Biol. Chem. **49**:187 (Nov.) 1921.

13. Mayer, R.: Calcium Content of Blood in Children, Arch. f. Kinderh. **70**: 170 (Dec.) 1921.

14. Nohlen, A.: Blood Calcium in the Mother and New-Born, Ztschr. f. Kinderh. **42**:60, 1926.

15. Leicher, H.: Action of Endocrines on Serum Calcium, Deutsches Arch. f. klin. Med. **141**:85 (Nov.) 1922.

a level of the serum calcium but rather the amount of diffusible calcium, as proposed by Moorhouse and Cameron,[16] or the concentration of the calcium ions available for utilization by the body. The diffusible fraction is that portion of the blood calcium that is capable of passing through the capillary wall and cell membrane. Liu,[17] utilizing a method of combined ultrafiltration and dialysis, found that this portion may be low even in the cases of relatively high total serum calcium. He believes that it is this form of diffusible or ionic calcium that controls the nervous symptoms. He further demonstrated that parathyroid extract and other measures employed in controlling tetany produced an increase in diffusible calcium that was out of proportion to the total rise.

Apparently, the syndrome illustrated in the six cases herewith presented is the result of a qualitative rather than a quantitative diminution of the serum calcium. From the improvement noted following the administration of parathyroid extract, it is very likely that this clinical entity is dependent on a condition of hypoparathyroidism.

The Southwest Clinic, 1717 Pacific Avenue.

16. Moorhouse, V. H. K., and Cameron, A. T.: The Tetany and Parathyroid Deficiency and the Calcium of the Blood and the Cerebrospinal Fluid, J. Biol. Chem. **63**:687 (April) 1925.

17. Liu, S. H.: Chronic Juvenile Tetany; Comparative Study of the Effects of Various Treatments on the Calcium and Phosphorus Metabolism in Tetany, J. Clin. Investigation **5**:259 (Feb.) 1928; Partition of Serum Calcium into Diffusible and Non-Diffusible Portions, Chinese J. Physiol. **1**:331 (July) 1927.

SOFT CURD MILK

HERBERT L. ELIAS, M.D.
ROCKVILLE CENTRE, N. Y.

Hill,[1] in 1928, reported a test for quantitatively measuring the difference in toughness of curds in cow's milk. Briefly, this test consisted of measuring, on a gram scale, the pull required to draw a star-shaped knife through a curd formed by adding a solution of pepsin to milk. He found that the curd tension may vary from 16 to 140 Gm., the average being 60 Gm. Any milk with a curd tension of less than 30 Gm. he called a "soft curd milk," and all above 30 Gm. "hard curd milk." This standard has been adopted by the department of health of New York City. It seems well established by the investigations of Hill that the toughness of the curd is an individual characteristic and is fairly uniform and permanent for the individual cow. Hill [2] suggested that soft curd milk is better tolerated by infants than is hard curd milk.

Attempts at modifying the curd in cow's milk have been popular for many years, and the importance of the curd in infant feeding has been stressed within the past two years by Brennemann.[3] He believes that the alleged advantages of lactic acid milk are due not to its improved buffer qualities, but to the softness of the curd. It would seem that a milk with a natural soft curd should have some advantage over a milk the curd of which was rendered soft artificially.

Brennemann [4] in 1913, pointed out how unreliable deductions from test tube experiments are for revealing what actually goes on in the infant's stomach. My observations on the use of soft curd milk have seemed to strengthen this opinion.

Through the cooperation of the Sheffield Farms Company it has been possible to use soft curd milk in the well baby ward at Bellevue Hospital. This ward contains, on the average, thirty patients varying in age from newly born to 2 years. The patients are admitted as premature

---

From the Department of Pediatrics of New York University and The Children's Medical Service of Bellevue Hospital.

1. Hill: Bull. 227, Utah Experimental Station, Logan, Utah.
2. Hill, Rubin L.: Soft Curd Milk: Nature's Food for Infants, Arch. Pediat. **48**:417 (July) 1931.
3. Brennemann, Joseph: The Curd and Buffer in Infant Feeding, J. A. M. A. **92**:364 (Feb. 22) 1929.
4. Brennemann, Joseph: Boiled Versus Raw Milk: An Experimental Study of Milk Coagulations in the Stomach, J. A. M. A. **60**:575 (Feb. 22) 1913.

infants, as well infants whose mothers are patients in the hospital or as foundlings. The infants, as a rule, receive whole milk, water and sugar (dextrimaltose, dextrose, corn syrup or sucrose) mixtures. The caloric intake varies from 45 to 65 calories per pound depending on the need for growth. Most of the infants receive a supplement of orange juice and cod liver oil, cereals after the fourth month and vegetables after the sixth month.

Over a period of six months, soft curd milk was substituted for other milk in the diet of babies selected for this study. The rest of the diet was unchanged. The patients were selected at random, except that preference was given to small and underweight infants. All patients were under 1 year of age, and over 90 per cent under 6 months. Infants received soft curd milk over a period of from ten to ninety days, with an average of twenty-one days. Because of the large number of admissions, it was not possible to keep infants in the ward after they were ready for discharge, and therefore the period of observation was not always as long as is desirable.

EXPERIMENTAL DATA

Size of the Curd.—The size of the curd of soft curd milk, evaporated milk, certified milk and breast milk was compared after the milk had been in the infant's stomach fifteen, thirty and sixty minutes. The infant's stomach was emptied either by a small-sized stomach tube or by accidental vomiting. Determinations of the p_H of the gastric contents were also made, and the relation between gastric acidity and size of the curd was investigated. I am aware, as pointed out by Brennemann, that observations on the size of curds passed through a stomach tube are open to criticism, particularly the small tube that must be used on an infant, and an attempt was consequently made to induce vomiting.

An arbitrary standard of curd size and consistency was set up as follows: Milk that flowed out of the tube or the mouth easily and without any curdling was called liquid (L); that which had a very slight flocculent precipitate was called normal (N); that with very small but definite curds, 1 plus, with larger curds, 2 plus and with very large curds, 3 plus.

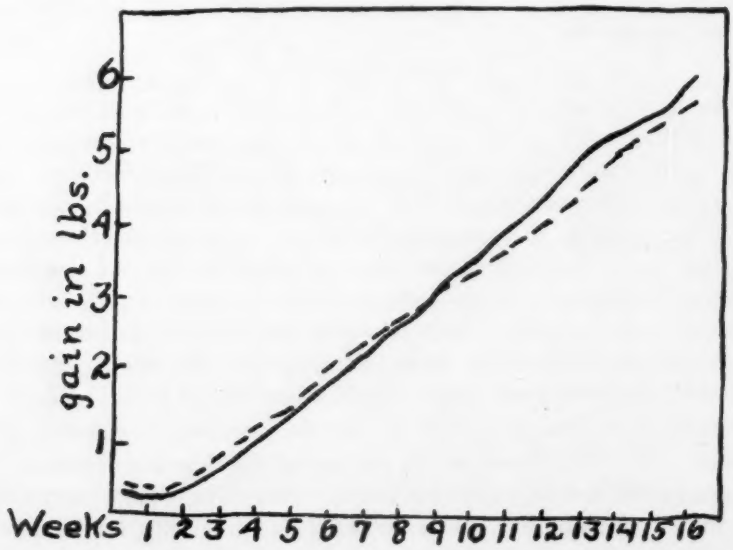
The results are shown in table 1. Soft curd milk in the baby's stomach formed curds about equal in size to those formed from boiled certified milk but much softer than those from raw certified milk. However, soft curd milk does not invariably give soft curds, for in nine (16 per cent) of fifty-four determinations, this milk showed large firm curds. Contrary to Hill's findings, soft curd milk showed a higher percentage of hard curds than did boiled milk. It is interesting to note that the curd of evaporated milk approaches that of breast milk in quality.

No curd at all was found on three determinations with soft curd milk fifteen minutes after feeding. As has been previously observed, the curds were larger after thirty minutes and one hour than during the first thirty minutes after feeding.

No difference in the gastric p_H [5] with hard or soft curd milk was found. The average p_H of the gastric contents containing hard curds was 6.2, and of that containing soft curds, 5.8.

TABLE 1.—*Comparison of the Size of the Curd Formed by Various Milks*

Kind of Milk	Number of Observations	Character of Gastric Contents		
		Liquid	Soft Curd N +	Hard Curd 2+ and 3+
Certified, unboiled	27	..	6	21
Certified, boiled	54	..	51	3
Soft curd, unboiled	54	3	41	9
Evaporated	12	8	4	..
Breast	10	9	1 (N)	..



Normal weight curve (solid line), and composite weight curve (dash line), of babies gaining on soft curd milk.

Weight Curves.—Eighty-two babies received soft curd milk instead of ordinary certified milk. In this group fifty-four (65 per cent) gained weight at the expected rate of well babies, as can be seen from the composite weight curve. The average caloric intake for these babies was 61 calories per pound.

5. The gastric p_H was done by the colorimetric method described by Clark. Clark, J. M.: Determination of Hydrogen Ions, Baltimore, Williams & Wilkins Company, 1925, p. 24.

Twenty-one babies (26 per cent) lost weight, and in this group the average energy quotient was 51 calories per pound. This group includes some of the babies in whom infections developed and all of the babies who died of gastro-intestinal indigestion. The chief cause of failure to gain was vomiting and diarrhea, which were considered to show gastro-intestinal indigestion either mild or severe; the next most common cause was respiratory infection, and in a few instances too low caloric intake.

No definite change in the weight curve was effected by a change from certified milk to soft curd milk. No effect was seen in the babies who failed to gain on soft curd milk by a change to certified milk.

Vomiting and Diarrhea.—It was noticed early in this study that when a change was made from boiled certified to soft curd milk there was a slight increase in the number of stools. This is a common observation when babies are changed from boiled to unboiled milk of any kind. The stools were a little looser and contained a few more curds. The amount

TABLE 2.—*Comparison of the Number of Cases of Intestinal Intoxication in Infants Receiving Soft Curd Milk with the Number in Those Receiving Other Milk*

Kind of Milk	Patients in Whom Gastro-Intestinal Intoxication Developed		Patients Dying of Gastro-Intestinal Intoxication	
	Number	Per Cent	Number	Per Cent
Soft curd (82)	14	17	5	6
Certified, lactic acid evaporated (400)	96	24	63	15

of unimportant vomiting and regurgitation that all babies manifest from time to time was as frequent in babies fed with soft curd milk as in those fed with other milk. This vomiting includes that due to feeding too large a volume, feeding too slowly or failure to hold the baby up after feeding to expel swallowed air.

The number of babies in whom gastro-intestinal indigestion of mild or severe type developed was slightly less than in a control group of 400 cases. In the series fed soft curd milk, indigestion of either the mild or severe type developed in fourteen (17 per cent); 5.9 per cent of the babies receiving this type of milk died of intoxication. In a larger series in which certified milk was mostly given, gastro-intestinal intoxication developed in 24 per cent, and 15.7 per cent died. In the studies of soft curd milk, all of the babies who died were less than 1 month of age. However, the difference was so small that one would hesitate to prescribe soft curd milk either as a prophylaxis or as a treatment for digestive disturbance. I was unable to find in any case that soft curd milk per se would relieve vomiting or diarrhea.

Soft curd milk was fed to only two premature infants. In both these babies vomiting and diarrhea developed, and both died. Obviously, no conclusions can be drawn from two cases.

SUMMARY

1. Eighty-two babies received soft curd milk for periods of from ten to ninety days. The size and consistency of the curds in the infants' stomachs were compared with those in the curds from certified milk (boiled and unboiled), evaporated milk and breast milk.

2. The curds in the infants' stomachs after taking soft curd milk were usually softer than those after taking unboiled certified milk, about equal in size to those of boiled milk, but larger and tougher than those of evaporated or breast milk.

3. Soft curd milk was of no special value in preventing or treating vomiting and diarrhea.

4. This study indicates that soft curd milk has no decided advantages over other certified milks in its digestibility, and that it has no unusual tendency to make infants gain weight. The infants given soft curd milk, in fact, needed a higher caloric intake than those given other milks.

EFFECT OF TONSILLECTOMY AND ADENOIDECTOMY ON IMMUNITY TO DIPHTHERIA

NOEL G. SHAW, M.D.
CHICAGO

Impressed by numerous observations that diphtheria is relatively infrequent in tonsillectomized persons, Schick and Topper [1] of New York studied the effect of tonsillectomy on the production of immunity to diphtheria. They reported that among 100 children who were susceptible to diphtheria, as determined by a positive Schick test just before the operation, 82 per cent gave a negative reaction when retested six months after tonsillectomy. This percentage held true for children under 6 years of age as well as for the older group of children from 6 to 12 years. These authors believe that only a small percentage of a control group could be expected to give negative reactions to the Schick test in a like period of time. The normal expectancy of negative reactions in children, according to the combined figures of Park and Zingher, von Groer and Kassowitz (as presented by Schick and Topper), increases from 16.8 per cent in the first to third years to 76.4 per cent in the twelfth to thirteenth years.

Schick and Topper also made Schick tests consecutively on 200 children who had undergone tonsillectomy before entering Mount Sinai Hospital. Of these, 81 per cent were negative; and even in the group under 6 years, 75 per cent were negative. Accordingly, Schick and Topper concluded that tonsillectomy in some way favors "the development of a humoral immunity against diphtheria." They pointed out that the immunity might develop from a mild unrecognized diphtheria after tonsillectomy, or, according to Hirszfeld's [2] hypothesis, by the general production of antibodies following infection, as in the tonsillar fossae after operation, or, according to Opitz' [3] theory, by the stimulation to antitoxin production following the minute quantity of toxin contained in the Schick test.

From the Department of Pediatrics, Rush Medical College of the University of Chicago, and from the Cook County Hospital.

Aided by grant from the John McCormick Institute for Infectious Diseases.

1. Schick, Béla, and Topper, Anne: Effect of Tonsillectomy and of Adenoidectomy on Diphtheria Immunity, Am. J. Dis. Child. **38**:929 (Nov.) 1929.

2. Hirszfeld, Hanns; Hirszfeld, L., and Brockman, H.: On the Susceptibility to Diphtheria (Schick Test Positive) with Reference to the Inheritance of Blood Groups, J. Immunol. **9**:571 (Nov.) 1924.

3. Opitz, H.: Klin. Wchnschr. **6**:1701, 1927.

Geddie [4] studied the results of Schick tests on 883 children in Rochester, Minn., a city of 20,000 with a low incidence of diphtheria (thirty cases in the previous five years). Of 411 children from 1 to 18 years of age used as controls (no tonsillectomy, diphtheria or immunization), 13.6 per cent gave negative reactions. Among 96 children of similar ages with no difference in history from the previous group except that tonsillectomy had been performed more than six months previously, 20.8 per cent of the tests were negative, an increase of 7.2 per cent in negative reactions in the group operated on. Two other groups, with an added factor in each of some immunization against diphtheria, showed about an equal percentage of negative reactions, 75 per cent, whether the tonsils had been removed or not. Geddie concluded that tonsillectomy had no effect on humoral immunity against diphtheria in a small community.

TABLE 1.—*Original Tests*

	White		Negro		Mexican	
Age	Males	Females	Males	Females	Males	Females
1 to 5 years	22	5	6	3	3	1
6 to 10 years	34	30	18	8	1	3
11 to 15 years	16	15	3	6		
Totals	72	50	27	17	4	4

The 174 children in the present study came from the wards of Cook County Hospital [5] from time to time during the period from January to October, 1930. With the exception of 9 children from the suburbs, they were from the crowded districts of Chicago. There were 122 white, 44 Negro and 8 Mexican children, from 18 months to 15 years of age, the majority being between 6 and 12 years. Fifty-nine per cent were boys.

Schick tests were done on this group to find the percentage of negative reactions. A history was taken of previous attacks of diphtheria, immunization or exposure, and the presence of tonsils was noted. The results of the tests in children with and without tonsils were tabulated. A smaller group of children with positive Schick tests before tonsillectomy was retested from six to fourteen months after the operation, and the results were compared to those in a control group that had not undergone tonsillectomy. The Schick tests were done with material known to be potent as shown by tests made in the John McCormick Insti-

4. Geddie, Kenneth: Effect of Tonsillectomy and Adenoidectomy on Diphtheria Immunity, Am. J. Dis. Child. **40**:1032 (Nov.) 1930.

5. Service of Dr. Maurice L. Blatt, chief of staff, Cook County Children's Hospital.

tute for Infectious Diseases and readings made forty-eight hours later. Controls of heated Schick test material were used. All tests and readings were done by me so as to rule out the factor of personal variation.

RESULTS OF ORIGINAL SCHICK TESTS

To determine if there is a higher percentage of negative reactions to the Schick test in children with tonsils removed than in those not operated on, the other factors that would tend to influence immunity to diphtheria must be ruled out. Therefore, from each group one excludes those whose negative reactions might be explained by a history of diphtheria or unrecognized diphtheria following a specific exposure to the disease or some form of immunization.

TABLE 2.—*Summary of Original One Hundred and Seventy-Four Schick Tests*

	Tonsils Not Removed				Tonsils Removed (Over 6 Months Previously)			
	No Immunization		Immunization		No Immunization		Immunization	
Age	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative
1 to 5 years	18	12	2	3	2	1	2	..
6 to 10 years	42	21	8	9	5	5	3	1
11 to 15 years	17	10	8	5	..	..	..	..
Totals	77	43	18	17	7	6	5	1

Tonsils not removed	155	Tonsils removed more than 6 months previously	19
Negative reactions to Schick test	60	Negative reactions to Schick test	7
Total percentage of negative reactions	38.7	Total percentage of negative reactions	36.9
Negatives as possible result of immunization, etc.	17	Negatives as possible result of immunization	1
Unexplained negative reaction to Schick tests	43	Unexplained negative reaction to Schick tests	6
Percentage of unexplained negative reactions	31.1	Percentage of unexplained negative reactions	33.3

Among 155 children with tonsils, 60, or 38.7 per cent, gave negative reactions to the Schick test. In this group, more than six months previously, 35 had had diphtheria, had had one or more injections against diphtheria or had been exposed to the disease and had received a prophylactic injection of diphtheria antitoxin. (Still, 18 of the 35 showed positive reaction to the test, indicating that complete immunization had not been afforded.) If the 17 children who thus gave negative reactions with plausible explanation are excluded, there are 43 of 138 children, or 31.1 per cent, with negative reactions to the Schick test for no apparent reason. Geddie found only 13.6 per cent with negative reactions in a similar group of 411 children from a rural community.

It is doubtful if any child spontaneously gives a negative reaction to the Schick test, unless he inherits sufficient immunity from an immune mother. It is conceivable that children who give negative reactions for

no apparent reason have actually had mild unrecognized diphtheria at some time. Accordingly, one would expect to find more such negative reactions among children from a crowded district where chances of infection are greater.

The control group of 19 children with tonsils removed more than six months before the original Schick test was made is too small for any

TABLE 3.—*Retests of Patients Originally Giving Positive Reactions*

Age	White		Negro	
	Males	Females	Males	Females
1 to 5 years	5	2	..	1
6 to 10 years	13	8	3	1
11 to 15 years	6	4	1	5
Totals	24	14	4	7

TABLE 4.—*Results of Retests of Patients Originally Giving Positive Reactions*

	Tonsils Removed											
	Tonsils Removed After Original Schick Test				Tonsils Removed Over 6 Months Before Original Schick Test				Tonsils Not Removed			
	No Immunization		Immunization		No Immunization		Immunization		No Immunization		Immunization	
Age, Years	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative
1 to 5	2	..	..	..	1	..	..	..	2	1	1	1
6 to 10	12	1	4	1	1	..	..	..	4	..	2	..
11 to 15	13	1	..	..	..	..	..	..	2	..	..	..
Totals	27	2	4	1	2	..	..	..	8	1	3	1

Total number of children retested 49
Tonsils removed before original Schick test (not counted) 2

Tonsils removed after original Schick test 34
Total negative reactions to Schick test. 3
Total percentage of negative reactions. 8.8%

Negative as possible result of immunization or questionable diphtheria..... 2
Unexplained negative reactions to Schick test..... 1
Percentage of unexplained negative reactions..... 3.1%

Tonsils not removed..... 13
Total negative reactions to Schick test. 2
Total percentage of negative reactions. 15.3%

Negative as possible result of immunization or questionable diphtheria..... 2
Unexplained negative reactions to Schick test..... 0

definite conclusions. Six of the 19 children had had diphtheria or some form of immunization to diphtheria more than six months previously, but only 1 actually had a negative reaction. Excluding this 1, 33.3 per cent of the control group were negative to the Schick test without explanation. This result corresponds closely to that in the group of children with tonsils. Among a similar group of 200 New York children whose tonsils had been removed, Schick and Topper reported that 81 per cent had a negative reaction to the Schick test, but they neglected to state if any had had previous immunization or diphtheria.

RETESTS

To determine the effect of tonsillectomy and adenoidectomy on children who had previously given a positive reaction to the Schick test the tests were repeated from six to fourteen months after the operation. This afforded plenty of time for immunity to develop as the result of tonsillectomy, if this was possible. Forty-nine children with originally positive reactions returned for further tests. All of these children were from the crowded districts of the city. There were 37 white and 12 Negro children, of ages and sex groups corresponding approximately to the group originally tested.

Two of the children had had their tonsils removed more than six months before the original test. In order not to include children perhaps giving persistently positive reactions after tonsillectomy, these 2 are excluded from the calculations.

Of 34 children with positive reactions to the Schick test who underwent tonsillectomy and adenoidectomy, and returned as mentioned, only 3, or 8.8 per cent, gave negative reactions. One had had a questionable case of diphtheria (severe throat infection and malaise) following tonsillectomy, and another had had three injections of diphtheria toxin-antitoxin four months previously. One child's reaction had become negative without any apparent reason except the tonsillectomy.

In a control group of 13 children not operated on, the reactions of 2 had become negative. One of these had had three injections of diphtheria toxin-antitoxin six months previously; the other had had a questionable case of diphtheria. These results do not confirm those of Schick and Topper, who reported that in 82 per cent of their group the reactions to the Schick test turned negative six months after tonsillectomy and adenoidectomy.

SUMMARY

Schick tests were made on 174 city children. Of 155 with tonsils, 31.1 per cent gave negative reactions without obvious explanation; of 19 children with tonsils removed, 33.3 per cent gave negative reactions, as compared to 81 per cent as reported by Schick and Topper; of 34 children with positive reactions to the Schick test before tonsillectomy, 8.8 per cent gave negative reactions in from six to fourteen months after the operation, as compared to 82 per cent as reported by Schick and Topper. These results do not indicate that among city children tonsillectomy and adenoidectomy produce a humoral immunity against diphtheria as measured by the Schick test.

636 Church Street, Evanston, Ill.

UREA CLEARANCE TESTS

THEIR LIMITATIONS AS A MEASURE OF RENAL FUNCTION IN CHILDHOOD

L. EMMETT HOLT, JR., M.D.
BALTIMORE

It has been clearly demonstrated by Van Slyke [1] that measurements of urea excretion may indicate impairment of renal function some time before retention of urea in the blood occurs. The most recent modification of the Ambard coefficient—the urea clearance of Van Slyke—is used as a routine procedure in many medical clinics, and is generally regarded as the most sensitive of renal function tests. Although McIntosh, Möller and Van Slyke [2] presented data on urea clearance in childhood, this test has not come into general use for young children, and the question may well be raised as to whether the pediatrician is not neglecting a valuable and relatively simple procedure.

The purpose of this article is to call attention to certain limitations that affect this test when applied to children, some of which were not emphasized in the publication of McIntosh, Möller and Van Slyke. No new data are presented; my conclusions are drawn entirely from an analysis of the data of the aforementioned authors.

The relation between the excretion of urea and the volume of the urine has been studied extensively by Van Slyke and his collaborators.[3] When the volume of the urine is small or moderate, the concentration of urea in the urine bears an almost constant ratio to the concentration of urea in the blood; alterations in the volume of the urine have comparatively little influence on the concentration of urea in the urine, and the total output of urea increases with the urinary volume. If, however, the urinary volume exceeds a certain critical point, which Van

---

From the Harriet Lane Home of the Johns Hopkins Hospital and the Department of Pediatrics of the Johns Hopkins Medical School.

1. Van Slyke, D. D.: Medicine **9**:257, 1930.

2. McIntosh, J. F.; Möller, Eggert, and Van Slyke, D. D.: J. Clin. Investigation **6**:467, 1929.

3. Austin, J. H.; Stillman, E., and Van Slyke, D. D.: J. Biol. Chem. **46**:91, 1921. Möller, Eggert; McIntosh, J. F., and Van Slyke, D. D.: J. Clin. Investigation **6**:427, 1929.

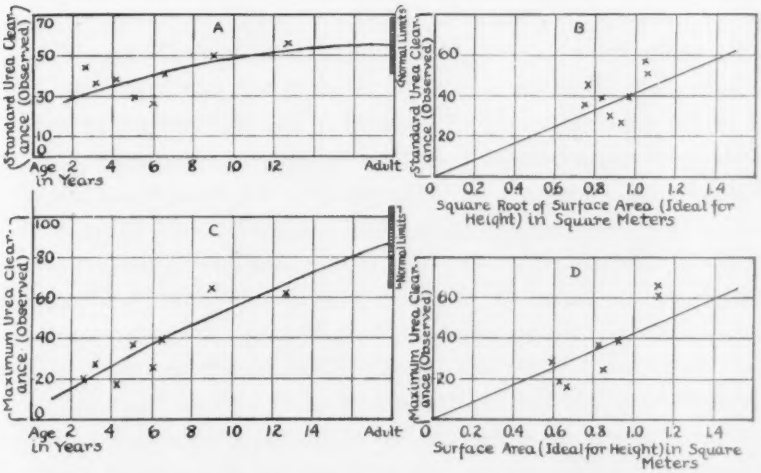


Chart 1.—*A*, curve for the standard urea clearance as a function of age. *B*, curve for the standard urea clearance as a function of surface area. *C*, curve for the maximum urea clearance as a function of age. *D*, curve for the maximum urea clearance as a function of surface area.

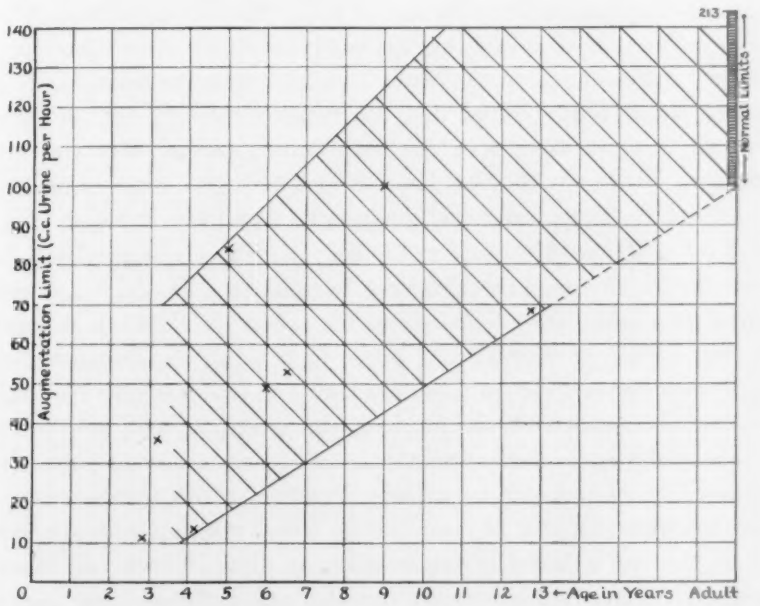


Chart 2.—Augmentation limit for the excretion of urea in children. (From the data of McIntosh, Möller and Van Slyke.)

Slyke has called the augmentation limit, no further increase in the total excretion of urea occurs; further increases in the urinary volume merely diminish the concentration of urea in the urine. Below the augmentation limit, Van Slyke and his collaborators measured renal function by the expression: $\frac{U}{B}\sqrt{V}$, known as the standard urea clearance, and above the augmentation limit they employed the expression $\frac{U}{B}V$, the maximum urea clearance ($\frac{U}{B}$ being the ratio of urine urea concentration to blood urea concentration, and V the volume of urine in cubic centimeters per minute). In the adult the augmentation limit is relatively constant; it was found by Möller, McIntosh and Van Slyke [3] to vary between 100 and 213 cc. per hour. By making observations above or below these limits, one may readily determine either the maximum clearance or the standard clearance, as may be desired.

When one examines the data of McIntosh, Möller and Van Slyke on children, it is apparent that lower values for standard and maximum clearance are obtained, particularly in the younger children. Assuming that renal function is proportional to surface area, these authors have introduced a correction, but the corrected urea clearances, although of the same general magnitude as the adult figures, show a far greater fluctuation in the eight children studied than do urea clearances in a much larger series of adults. In only five of these children did the corrected clearances fall within the limits for the normal adult. When one plots the urea clearances against body weight or (as we have done in chart 1) against age, these greater variations from the normal average persist. It is worth noting that the relation between age and urea clearance is quite as constant as that between surface area and urea clearance. However, the fact remains that urea clearances in children are subject to greater individual fluctuations than those in adults.

A more serious drawback to the use of urea clearance tests is the variability of the augmentation limit in children. In chart 2 I have plotted the augmentation limit against the age of the child. It is apparent that a child of 4 years may prove to have an augmentation limit anywhere between 10 cc. of urine per hour (an exceptionally low secretion for this age) and 80 cc. per hour (an unusually high rate). The physician who would study urea clearance in such a child is faced with the necessity of maintaining urinary secretion at one or the other of these extremes, or else of ascertaining where the augmentation limit actually lies by a series of observations at different rates of urinary secretion. When one comes to consider children below the age of

3 years, the latter course would seem to be a necessity. One hesitates by extrapolation on the chart to estimate what the variations in augmentation limit may be at this time of life.

COMMENT

There is no reason to doubt that the urea clearance in children is as sensitive an index of renal function as in adults. However, the extended observations that may be necessary to determine the augmentation limit and the greater variability of the clearance values in normal subjects are serious limitations to the usefulness of this test.

AURICULAR FIBRILLATION IN CHILDHOOD

HERBERT W. SCHMITZ, M.D.
NEW YORK

Auricular fibrillation is a common arrhythmia in adults. According to White,[1] it probably ranks third in order of frequency, premature contractions being first and paroxysmal tachycardia second. In children this form of arrhythmia has been regarded as extremely uncommon, and reports of only a few cases in children under 10 years of age appear in the literature (Price and Mackenzie,[2] Sutherland and Coombs,[3] Ehrenreich,[4] Ogden,[5] Resnik and Scott,[6] Leys and Russell,[7] Sidel and Dorwat,[8] Barber and Middleton,[9] Schwartz and Weis [10]). The number recorded in patients between the ages of 10 and 17 years is somewhat larger (Barber and Middleton,[9] Schwartz and Weiss,[10] Cookson [11]).

Most of the cases described had their onset in the course of an active rheumatic carditis or were observed in association with inactive rheumatic cardiovalvular disease. The impression is received that the outlook is extremely grave, and that if the condition is survived, the child is usually confined to bed with a greater or less degree of congestive failure.

From the Convalescent Home for Cardiac Children, Irvington, N. Y., service of Dr. Robert H. Halsey.

1. White, P. D.: Heart Disease, New York, The Macmillan Company, 1931.

2. Price, F. W., and Mackenzie, I.: Heart **3**:233, 1911-1912.

3. Sutherland, G. A., and Coombs, C. F.: Heart **5**:15, 1913-1914.

4. Ehrenreich, S. G.: New York M. J. **99**:269, 1914.

5. Ogden, R. T.: Auricular Fibrillation: Case in Child Aged 10 Years, Am. J. Dis. Child. **29**:767 (June) 1925.

6. Resnik, W. H., and Scott, W. J.: Auricular Fibrillation: Report of Case in Child Aged 4 Years, Am. J. Dis. Child. **31**:357 (March) 1926.

7. Leys, G. O., and Russell, H. B.: Lancet **2**:702, 1927.

8. Sidel, N., and Dorwat, F. G.: Boston M. & S. J. **196**:216, 1927.

9. Barber, E. W., and Middleton, R. P. Auricular Fibrillation in Childhood: Report of Cases, Am. J. Dis. Child. **35**:420 (March) 1928.

10. Schwartz, S. P., and Weiss, M. M.: Auricular Fibrillation in Children: Its Relation to Rheumatic Heart Disease, Am. J. Dis. Child. **36**:22 (July) 1928.

11. Cookson, H.: Lancet **2**:1139, 1929.

CLINICAL OBSERVATIONS

During a five year period, from 1926 to 1931, nineteen cases of auricular fibrillation were observed among a total of 1,345 children with heart disease admitted to Irvington House (table). Fibrillation was present in fifteen of these children at the time of admission, and in four the irregularity developed while they were under observation at the home. The patients were about evenly divided as to sex, there being ten girls and nine boys. The ages ranged between 8 and 16 years at the time the fibrillation was noted. Seventeen of the nineteen children gave a history of having had one or more attacks of rheumatic infection. Thirteen had had two or more attacks, one child having had eight attacks. In two children heart disease was noted several years before the first recorded attack of rheumatic fever. It is recognized, however, that in children it is often difficult to obtain a history of rheumatic infection, since at this age the rheumatic manifestations are not always clearly defined. In the remaining seventeen cases, heart disease was discovered either in the same year that rheumatic fever occurred or from one to six years later. Mitral stenosis and insufficiency were present in all the children, and, in addition, a diagnosis of aortic insufficiency was made in six or one third of the cases.

Auricular fibrillation was first noted from one to ten years after the discovery of valvular heart disease. In none of these children could the onset of auricular fibrillation be attributed to the use of digitalis, since, so far as can be ascertained, no digitalis was administered prior to the onset of the total irregularity. After the appearance of fibrillation, digitalis was given only when required to relieve a congestive failure and to maintain the ventricular rate at 80 beats or less per minute.

The youngest child in whom fibrillation was observed was 8 years of age. One child was 11, two were 12, three were 13, four were 14, five were 15, and three were 16 when auricular fibrillation was discovered.

Of the nineteen children, seven are now dead. In case 1, fibrillation occurred during a recurrent attack of rheumatic fever and carditis and continued for a period of ten days, but the child died twenty-one days after the return of normal sinus rhythm. In case 2 the patient lived seventeen days after auricular fibrillation was first noted; in case 3, ninety days; in case 4, fourteen months; in case 5, twenty-four months; in case 6, thirty months, and in case 7 forty-four months. An active rheumatic infection was present in cases 1, 2, 3, 4, 5, 6 and 7 at the time auricular fibrillation was first observed, and was still present up to the time of death in cases 1, 2, 3 and 4.

Of the twelve patients that are still alive, an active carditis was present in four at the time the total arrhythmia was first diagnosed. No

evidence of active disease was observed in the remaining eight. There has been no recurrent infection in any of these cases since the discovery of auricular fibrillation. An active carditis is, however, still present at the time of this report in the patients in cases 9 and 10, since they have an elevated temperature, leukocytosis, anemia and signs of congestive failure.

The average duration of life after the total irregularity was noted in the seven patients that have died was sixteen months; the shortest duration was seventeen days, and the longest forty-four months.

The duration of the arrhythmia in the twelve children still living averages about thirty-one months at the time of this report. These children can be separated functionally into four groups: two children with active infection not classified functionally; five belonging to class IIA; four belonging to class IIB, and one belonging to class III.

INCIDENCE

In this series of children, auricular fibrillation appears to have occurred more frequently than the earlier literature would indicate. There were nineteen cases (1.4 per cent) in a total of 1,345 children with heart disease admitted to Irvington House in a five year period. Cookson [11] reported thirty "child" cases, or 2.5 per cent, in a total of 1,164 patients with auricular fibrillation admitted to the London Hospital. He also included five outside cases in his study. Schwartz and Weiss [10] stated that auricular fibrillation is not uncommon in children with rheumatic heart disease. They observed ten cases in sixty children with chronic rheumatic cardiovalvular disease admitted to the wards of the Montefiore Hospital during a five year period. They attributed the higher apparent incidence to more careful investigation. It is obvious, however, that the percentage of auricular fibrillation is likely to be higher in the hospital cases, since the hospitals usually receive patients with the severer types of cardiac disease, whereas the milder cases and the patients with inactive disease are more frequently referred to the cardiac convalescent homes. It must be granted, however, that a convalescent home that retains children with heart disease for considerable periods of time and maintains an efficient follow-up service affords an excellent opportunity for studying the incidence of this arrhythmia. Relatively few cases occur before the age of 10 years. We observed only one case in a child of 8 years; Schwartz and Weiss [10] reported five cases occurring at 10 years and under, and Cookson [11] none occurring in a child under 12 years.

In a general way it may be stated that in this small series there was an increasing number of cases with each increasing year in age.

ETIOLOGY

In adults, fibrillation of the auricles may be a complication of rheumatic heart disease, particularly after the development of mitral stenosis, coronary disease, essential hypertension, hyperthyroidism and such infectious diseases as acute rheumatic fever, lobar pneumonia, bronchopneumonia and diphtheria, and it may be caused by digitalis.

When auricular fibrillation occurs in children, it is almost always observed in the later course of either active or inactive rheumatic heart disease. Rheumatic fever was the cause of the heart disease in the thirty-five cases of auricular fibrillation reported by Cookson,[11] in ten cases cited by Schwartz and Weiss [10] and in the two cases reported by Barber and Middleton.[9] Price and Mackenzie,[2] however, reported a case of auriculoventricular block with fibrillation of the auricles following diphtheria.

In seventeen of the nineteen cases in this report the patients have had one or more attacks of rheumatic fever. The history of rheumatic infection was not obtained in two cases, but the character of the structural changes in the heart—mitral stenosis and insufficiency followed by a permanent total irregularity—justifies the diagnosis of rheumatic heart disease.

At the time the total irregularity was first observed in the cases here reported, an advanced involvement of the heart was noted, and this is also true of the series of cases cited by Schwartz and Weiss [10] and by Cookson.[11] In addition, active carditis was present in eleven of the nineteen children at the time of onset of the arrhythmia. In the remaining eight children, the inception of the irregularity was not observed, but there was no clinical or laboratory evidence of an active infection when the diagnosis of auricular fibrillation was made. Whether or not active carditis was present at the time of onset of the arrhythmia in the latter group of cases cannot be determined.

That the administration of digitalis may at times be responsible for the onset of a total arrhythmia has been conclusively proved. It was shown by Resnik [12] that the administration of large doses of the drug in severe myocardial failure in adults with cardiovascular hypertensive and syphilitic heart disease may produce a transient fibrillation of the auricles. Schwartz [13] cited two cases, both occurring in children, in which the administration of digitalis was held responsible for the development of auricular fibrillation during active carditis.

---

12. Resnik, W. H.: J. Clin. Investigation **1**:181, 1924.

13. Schwartz, S. P.: Digitalis Studies on Children with Heart Disease: Auricular Fibrillation in Children with Early Toxic Digitalis Manifestation, Am. J. Dis. Child. **39**:549 (March) 1930.

History and Important Findings in Nineteen Children with Auricular Fibrillation

Case	Rheumatic Infection Dates	Heart Disease Discovered Date	Onset Auricular Fibrillation Date	Infection at Time of Onset of Auricular Fibrillation	Infection to Time of Death	Infection Now Present	Valvular Lesion	Age Auricular Fibrillation Noted, Years	Duration Auricular Fibrillation	Age at Time of Death, Years	Present Age, Years	Present Condition of Patient
1	1928, 1930	1929	1930	Yes	Yes	....	Mitral insufficiency and stenosis	12	10 days	12	..	Dead
2	1921, 1930	1927	1930	Yes	Yes	....	Mitral insufficiency and stenosis, aortic insufficiency	13	17 days	13	..	Dead
3	1924, 1925, 1926, 1927, 1929	1924	1929	Yes	Yes	....	Mitral insufficiency and stenosis	8	90 days	8	..	Dead
4	1922, 1923, 1924, 1925, 1926, 1927, 1928, 1929	1922	1929	Yes	Yes	....	Mitral insufficiency and stenosis, aortic insufficiency	15	14 months	16	..	Dead
5	1923, 1928	1916	1928	Yes	No	....	Mitral insufficiency and stenosis, aortic insufficiency	16	24 months	18	..	Dead
6	1923, 1924, 1925, 1926, 1928	1923	1928	Yes	No	....	Mitral insufficiency and stenosis	11	30 months	14	..	Dead
7	1918, 1926	1925	1926	Yes	No	....	Mitral insufficiency and stenosis	14	44 months	18	..	Dead
8	1922	1924	1931	No	....	No	Mitral insufficiency and stenosis, aortic insufficiency	16	4 months	..	16	Class II B
9	1924, 1930	1925	1930	Yes	....	Yes	Mitral insufficiency and stenosis, aortic insufficiency	15	7 months	..	15	Active carditis
10	1924, 1929, 1930	1929	1930	Yes	....	Yes	Mitral insufficiency and stenosis	15	7 months	..	15	Active carditis
11	1919	?	1929	No	....	No	Mitral insufficiency and stenosis	15	24 months	..	17	Class II A
12	1926	1926	1929	No	....	No	Mitral insufficiency and stenosis	13	26 months	..	15	Class II A
13	?	1918	1928	No	....	No	Mitral insufficiency and stenosis	14	32 months	..	17	Class II B
14	1916, 1919, 1923, 1924, 1925, 1926, 1927	1922	1928	No	....	No	Mitral insufficiency and stenosis	15	35 months	..	18	Class II A
15	1922, 1923	1926	1928	No	....	No	Mitral insufficiency and stenosis	14	38 months	..	17	Class II A
16	?	1925	1927	No	....	No	Mitral insufficiency and stenosis	16	44 months	..	20	Class II A
17	1920, 1922, 1925, 1927	1924	1927	Yes	....	No	Mitral insufficiency and stenosis	13	48 months	..	17	Class II B
18	1926, 1927	1920	1927	Yes	....	No	Mitral insufficiency and stenosis	14	53 months	..	18	Class II B
19	1920	1920	1926	No	....	No	Mitral insufficiency and stenosis, aortic insufficiency	12	56 months	..	17	Class III

COURSE

The arrhythmia, once initiated, may run a chronic course. Transient or paroxysmal attacks lasting for days or weeks may occur in association with active infection, and the condition may also appear as a complication only in the last stages of active carditis.

PROGNOSIS

The prognosis of auricular fibrillation in childhood is determined by the nature of the underlying disease process. The duration of life after the onset or discovery of the arrhythmia is rather short according to various observers. In twenty-three cases cited by Cookson [11] the average length of life after the onset of the arrhythmia was ten months. In the series of ten cases described by Schwartz and Weiss,[10] four patients died within one week after the onset of auricular fibrillation; three died within one year; one lived twenty-two months and one almost four years, and one was still living but badly crippled with heart disease at the time the cases were reported. In the nineteen cases reported in this paper, seven patients have died. In this group the average length of life after the discovery of the arrhythmia was sixteen months. The average duration of the arrhythmia in the twelve children still living is approximately thirty-one months. Evidence of active carditis was present at the time of death in four of the seven children. Of these four children (cases 1, 2, 3 and 4), one lived seventeen days after the onset of the total arrhythmia; one (case 1, a child with paroxysmal auricular fibrillation lasting ten days) thirty-five days; one ninety days, and one fourteen months. The remaining three children, who had been free from active disease for some time, lived for a considerably longer period. One lived twenty-four months; one thirty months and one forty-four months. It is obvious that the activity of the rheumatic carditis is the important element in the outcome of the individual case. It is well known that congestive failure and death in children with heart disease rarely occur unless acute rheumatic carditis is present. Death may occur during the initial attack, but more often it occurs during a recurrent attack. With each recurrence additional cardiac damage results.

When the rheumatic infection has become quiescent, a much more hopeful outlook obtains. Of the twelve children that are still living, two have an active infection, and for that reason are confined to bed. Fibrillation of the auricles has been present for two months in one patient and five months in the other child. No evidence of an active process has been noted in the remaining ten children, and a total irregularity has been persistently present for from four to fifty-six months, or an average of approximately thirty-six months. The functional classification varies

in these cases. The patient in case 19 is the only child with congestive failure in whom the condition is considered as of class III. There are five cases of class IIA, and four of class IIB. In the group of children with fibrillation of the auricles but with no signs of an active infection the prognosis is dependent on the extent and degree of progress of the damage to the heart muscle.

Recurrences of rheumatic infection are more common during early childhood, and occur less frequently during the second half of the second decade of life than during the first half. In the ten children who are still alive and without signs of active infection there is no history of a relapse since the onset of the total arrhythmia, and all are now past 15 years of age. With the tendency to a change in the character of the disease process from an active to an inactive phase in later childhood, the outlooks seems brighter. In these cases the disease resembles that observed in adults. The ages at which the arrhythmia was first noted in the ten cases reported were from 13 to 16 years. The ultimate length of life will be determined by the integrity of the myocardium.

It is obvious that fibrillation of the auricles in childhood does not always indicate an immediate grave prognosis or an absolutely inactive or bedridden existence.

TREATMENT

The treatment for auricular fibrillation in children is influenced by three conditions: the presence of an active carditis, the functional efficiency of the heart and the ventricular rate. All cases should be carefully investigated for signs of activity. The rheumatic infection is readily recognized during the acute stage by the presence of an elevated temperature, an accelerated pulse rate and a leukocyte count of 10,000 or higher. During this acute phase the child should be kept at absolute rest. Following the acute stage there is often a period of low grade activity. As long as this is still evident, complete rest is indicated in spite of the absence of clinical symptoms. Any one of the following should be considered as possible manifestations of low grade activity: inertia and listlessness, a morning leukocyte count of 9,000 or over, an afternoon temperature of 100 F. (rectal) or higher, a ventricular rate persistently over 95 while the patient is at rest, inability to show improvement in tolerance for exercise and failure to gain weight.

When a congestive failure is present, adequate doses of digitalis are indicated no matter what the underlying pathologic condition. The dosage required to digitalize these patients is the same as that required in cases of fibrillation of the auricles in adults, approximately 0.15 cat units per pound of body weight. When the congestive failure is associated with active carditis, the response to digitalis is largely dependent on the severity of the infection. The outcome is uncertain as long as

there is an acute process present. The congestive failure is, however, often relieved by digitalis, as is evidenced by the prompt subsidence of objective signs and symptoms: improvement in breathing, disappearance of basal râles and edema of the ankles, decrease in the size of the liver and reduction of the ventricular rate. Patients with auricular fibrillation in whom the infectious process has become quiescent usually show a good response to digitalis when signs of congestive failure are present. After digitalization has been attained, 1 cat unit a day or every other day may be sufficient to maintain the ventricular rate between 70 and 80 beats per minute. The cases in which a recurrence of the disease develops, or those in which there is marked ventricular damage present a rather hopeless condition from the standpoint of treatment.

Quinidine may restore a normal sinus rhythm in certain cases, as was shown by Barber and Middleton [9] and Cookson.[11] It is, however, contraindicated in acute carditis and advanced heart failure.

SUMMARY

Auricular fibrillation in childhood is perhaps encountered more frequently than the earlier literature indicates. In children this form of irregularity is practically always associated with rheumatic heart disease. The incidence is greater in the second than in the first decade of life. The condition is observed in the course of either active or inactive advanced rheumatic heart disease. The arrhythmia, once established, may persist, or it may occur in short paroxysms and as a complication in the terminal stage of active carditis. The prognosis of auricular fibrillation in childhood is chiefly determined by the nature of the underlying disease process. Fibrillation of the auricles associated with active carditis indicates a grave prognosis. With a change in the character of the disease process from an active to an inactive phase in later childhood, a brighter outlook may be hoped for. The treatment for auricular fibrillation in childhood varies with the condition of the individual child. If active infection is present, absolute rest in bed and good nursing care are indicated. For congestive failure and rapid ventricular rate adequate doses of digitalis are administered. In the chronic form, associated with inactive rheumatic heart disease, the treatment is the same as for auricular fibrillation in adults.

ERYTHROBLASTIC ANEMIA

REVIEW OF CASES REPORTED SHOWING ROENTGENOGRAPHIC CHANGES IN BONES AND FIVE ADDITIONAL CASES

LEWIS A. KOCH, M.D.
AND
BENJAMIN SHAPIRO, M.D.
BROOKLYN

In 1925, Cooley and Lee [1] described five cases of anemia in children having unusual roentgenographic changes in the bones. Since this original description and a later report by the same authors,[2] much interest has been directed toward this condition. As other cases have been reported, difficulty has arisen in classifying this type of anemia. When Cooley described the peculiar changes in the bones occurring in his first cases, he stated that the anemia was not unlike that described by von Jaksch.[3] However, it is evident that clinicians continue to differ concerning the indefinite classification of von Jaksch's anemia. Many still apply the term loosely to that form of secondary anemia associated with faulty nutrition and prolonged infections. Since this confusion is so prevalent, it might be well to drop the term von Jaksch's anemia entirely. Cooley believed that his cases represented a form of hemolytic anemia due probably to a congenital defect in the hemolytopoietic system. Later reports and observations have tended to confirm this impression and to establish this form of anemia as a more definite clinical group. Cooley [4] later suggested that these cases be designated as erythroblastic anemia, and this term has been quite generally accepted.

Baty [5] defined the term erythroblastic anemia as follows: "An anemia which is a relatively uncommon condition, which has been

---

From the Department of Pediatrics, the Long Island College of Medicine, and the Long Island College Hospital.

1. Cooley, T. B., and Lee, Pearl: A Series of Cases of Anemia with Splenomegaly and Peculiar Bone Changes, Tr. Am. Pediat. Soc. **37**:29, 1925.

2. Cooley, T. B.; Witwer, E. R., and Lee, Pearl: Anemia in Children with Splenomegaly and Peculiar Changes in the Bones, Am. J. Dis. Child. **34**:347 (Sept.) 1927.

3. von Jaksch, R.: Ueber Leukämie und Leukocytose im Kindesalter, Wien. klin. Wchnschr. **2**:435 (May 30) 1889.

4. Cooley, T. B.: Likenesses and Contrasts in the Hemolytic Anemias of Children, Am. J. Dis. Child. **34**:1257 (Dec.) 1928.

5. Baty, J. M.: Anemia in Infants and Children, New England J. Med. **203**: 319 (Aug. 14) 1930.

separated recently from the heterogeneous group of so called von Jaksch's or splenic anemia. It is characterized by a congenital, familial and racial incidence, being limited to Mediterranean peoples; slowly progressing anemia with large numbers of nucleated red blood cells in the peripheral blood, enlargement of the spleen, mongoloid facies and distinctive changes in the bones as shown by X-ray examination."

It is probable that the characteristic gross and roentgenographic changes in the bones do not occur in every instance of erythroblastic anemia. Wollstein and Kreidel [6] recently reported nine cases which were apparently identical in their clinical manifestations and course, but only two evidenced the peculiar changes in the bones. Stillman [7] and Hitzrot [8] have also reported cases without evidence of the characteristic findings in the bones.

It has been shown that the changes in the bones are not pathognomonic of erythroblastic anemia alone. Friedman [9] and others [10] have seen these identical roentgenographic findings in cases of proved hemolytic icterus. Moore [11] and Vogt and Diamond [10] wrote of similar changes in cases of sickle cell anemia. It would seem that these changes are characteristic of the three hemolytic anemias: familial icterus, sickle cell anemia and erythroblastic anemia. In order to review the cases of erythroblastic anemia that have been reported, one would necessarily have to analyze carefully each report of unusual anemia found in the literature, including those designated as von Jaksch's anemia. Since the associated changes in the bones are so definite, we are presenting a summary of all of the cases of erythroblastic anemia with changes in the bones, including only the cases that have been reported in detail. Karshner,[11] in a recent article, mentioned that he

---

6. Wollstein, Martha, and Kriedel, K. V.: Familial Hemolytic Anemia of Childhood—von Jaksch, Am. J. Dis. Child. **39**:115 (Jan.) 1930.

7. Stillman, R. G.: A Study of von Jaksch's Anemia, Am. J. M. Sc. **153**:218 (Feb.) 1917.

8. Hitzrot, J. M.: Unclassified Type of Splenomegaly in Children, Ann. Surg. **88**:361 (Sept.) 1928.

9. Friedman, L. J.: Osseous Changes in Hemolytic Icterus, Am. J. Roentgenol. **20**:440 (Nov.) 1928.

10. Wade, R. B., and Steigrad, J.: Splenomegalic Jaundice with Associated Changes in the Skull, M. J. Australia **15**:530 (Oct. 27) 1928. Vogt, E. C., and Diamond, L. K.: Congenital Anemias Roentgenologically Considered, Am. J. Roentgenol. **23**:625 (June) 1930.

11. Karshner, R. G.: Roentgen Studies of the Bones in Certain Diseases of the Blood and Hematopoietic System, Am. J. Roentgenol. **20**:433 (Nov.) 1928. Moore, Sherwood: The Bone Changes in Sickle Cell Anemia with Note on Similar Changes Observed in Skulls of Ancient Mayan Indians, J. Missouri M. A. **26**:561 (Nov.) 1929.

Summary of Cases of Erythroblastic Anemia with Bone Changes Reported up to the Present Time

No.	Author	Sex, Age and Nativity	Familial Involvement	Age at Onset and Early Symptoms	Splenomegaly	Mongoloid Features, Age Noted	Hemoglobin, per Cent	Red Blood Cells	White Blood Cells	Normoblasts, per Cent	Fragility	Calcium and Phosphorus, Mg.	Course and Comment
1	Cooley, Witwer and Lee[2]	Female 3½ years Italian	Brother	10 months, with pallor, enlargement of abdomen and head	4 finger-breadths below costal margin	Yes 10 mo.	30	2,250,000	30,000 to 54,000	None	.....	.....	Syphilitic treatment; died 3 years after onset of symptoms
2	Cooley, Witwer and Lee[2]	Male 11 months Italian	Sister	8 months; change in color	3 finger-breadths below costal margin	Yes 2½ yrs.	48	2,520,000	12,500	Many later	Slightly decreased	5.0 very low	Treated with transfusions of blood and roentgen rays; died 2 years after onset of symptoms
3	Cooley, Witwer and Lee[2]	Male 2½ years Syrian	.....	4 months; restless, fretful, abdominal enlargement	Yes	Yes	35	2,020,000	18,000	5	.....	.....	Died 2½ years after onset
4	Cooley, Witwer and Lee[2]	Female 3 years English	No	Early infancy, with anemia and malnutrition	At umbilicus	Yes 5 yrs.	36	2,900,000	26,000	Many	Slightly decreased	8.0 1.6 later normal	Wassermann reaction of blood was 4 plus; syphilitic treatment given without improvement in anemia; alive 7 years after onset of symptoms
5	Cooley, Witwer and Lee[2]	Male 5 years Italian	No	8 months, with pallor and enlargement of abdomen	3 finger-breadths below costal margin	Yes 5 yrs.	56	4,170,000	13,900	Increase after splenectomy	Slightly decreased	Normal Normal	Splenectomy at 5 years of age; more anemic 3 years after operation
6	Cooley, Witwer and Lee[2]	Male 2¾ years Greek	Brother	2½ years, with pallor and enlargement of abdomen	2.5 cm. below umbilicus	Yes 2¾ yrs.	30	2,072,000	34,300	Increased	.....	.....	Course unchanged 2 months after first observation
7	Cooley, Witwer and Lee[2]	Male 1½ years Mulatto	No	1 year, with pallor and enlargement of abdomen	At umbilicus	No	35	3,200,000	12,200	7	Slightly increased	.....	Course unchanged 1 month after admission to the hospital
8	Hitzrot [8].....	Male 4 years	Yes	2 years, with pallor, jaundice and weakness	At crest of ileum	....	22	2,640,000	8,850	Frequent	0.5 and 0.25	.....	Splenectomy at 4 years followed by a persistent increase in normoblasts; 8 years after operation patient was quite well
9	Whipple, Reeves and Cobb: Ann. Surg. **88**: 380, 1928	Female 7 years Italian	Sister	3 years, with jaundice	Yes	Yes 7 yrs.	25	1,670,000	6,100	Few	Normal	9.05 5.0	Splenectomy; patient was quite well 14 months after operation
10	Whipple, Reeves and Cobb: Ann. Surg. **88**: 380, 1928	Female 3 years Italian	Sister	1½ years, with anemia and enlargement of abdomen	10 cm. below costal margin	Not definite	35	3,500,000	29,100	Many	Normal	.....	Transfusion of blood and splenectomy with some improvement
11	Wollstein and Krei-	Male	Brother	Since birth,	At crest of ileum	Yes	35	3,500,000	18,070	43	.....	.....	Splenectomy; observed for 5 years

	Cobb: Ann. Surg. **88**: 380, 1928	3 years Italian		enlargement of abdomen	costal margin								tomy with some improvement
11	Wollstein and Kreidel [6]	Male 4 years Greek	Brother	Since birth, with pallor and weakness	At crest of ileum	Yes 8 yrs.	35	3,500,000	18,070	43	.....	.....	Splenectomy; observed for 5 years after operation; anemic and condition poor when last observed
12	Wollstein and Kreidel [6]	Female 2 years Greek	Brother	21 months, with anorexia and loss of weight	7 cm. below costal margin	Yes	43	2,704,000	19,600	16	Normal	.....	Splenectomy was done followed by a persistent rise in normoblasts; died 4 years after operation
13	Baty [5].....	..... 11 months Greek	Twin	3 months, with pallor and enlargement of abdomen	Yes	Yes	..	.....	.....	.....	.....	.....	Treated by transfusions of blood; died 15 mos. after onset of symptoms
14	Baty [5].....	..... 11 months Greek	Twin	3 months, with pallor and enlargement of abdomen	Yes	Yes	..	.....	.....	.....	.....	.....	Treated by transfusions of blood; died 15 mos. after onset of symptoms
15	Baty [5].....	Male 8 years Greek	Brother	3 years	Yes	Yes 4 yrs.	..	.. ..	.....	.....	... .	.....	Alive 8 years after onset of symptoms
16	Baty [5].....	Male 7 years Greek	Brother	4 years	Yes	Yes 7 yrs.	..	.....	.....	.....	....	.....	Splenectomy; died a few months after operation
17	Capper, Aaron: Am. J. M. Sc. **181**: 620 (May) 1931	Female 3½ years Italian	No	7 months, with anemia	5 cm. below costal margin	No	22	1,900,000	21,300	35	Normal	....	Hemoglobin was maintained after splenectomy with persistent increase in normoblasts
18	Capper, Aaron: Am. J. M. Sc. **181**: 620 (May) 1931	Male 4 years Italian	No	2½ years, with weakness, pallor and loss of weight	1 cm. below umbilicus	Yes 2½ yrs.	10	1,700,000	10,000	Few	Slightly decreased	.....	Splenectomy; required transfusions of blood after operation
19	Authors' case 1.....	Female 3 months Italian	No	2 months, with pallor and jaundice	Moderately enlarged	Yes 7 mo.	66	4,000,000	34,000	9	Normal	10.8 6.0	Treated with transfusions of blood; died 15 mos. after onset of symptoms
20	Authors' case 2.....	Male 8 years Italian	Sister	Soon after birth, with pallor	At crest of ileum	Yes 5 yrs.	38	2,100,000	13,100	21	Normal	9.4 5.7	Treated with transfusions of blood; the anemia and weakness were more marked 6 mos. after admission
21	Authors' case 3.....	Female 5 years Italian	Brother	4 years, with pallor, jaundice and enlarged head	3 cm. below costal margin	Yes 4 yrs.	50	2,900,000	9,300	8	Normal	Normal Normal	Dietary and hygienic care; no improvement in 8 months
22	Authors' case 4.....	Male 10 months Italian	Questionable	4 months, with pallor and weakness	6 cm. below costal margin	Yes 6 mo.	45	2,900,000	15,000	10	Normal	Normal Normal	Transfusions of blood were given at frequent intervals; no improvement after 6 mos.
23	Authors' case 5.....	Female 9 years Italian	Sister	9 years, with pallor and weakness	10 cm. below costal margin	Yes 9 yrs.	45	2,390,000	8,800	16	Normal	Normal Normal	Not improved after 2 months

had observed two cases roentgenographically, and Vogt and Diamond [10] mentioned thirteen cases. Undoubtedly numerous others have been seen which have not been reported.

CLINICAL FEATURES

Erythroblastic anemia is probably familial. Of the eighteen cases with changes in the bones that have been summarized, ten have had a familial history. M. R. (case 3) in this report is a sister of R. R. (case 2) and was discovered only by examining all of the children in the family. M. B. (case 5) had an older sister who died of anemia. Nearly all of the cases reported have been in Mediterranean races, and the majority of the patients have been Italian. We have been unable to find any cases appearing in the foreign literature.

The onset is in early infancy. However, several of the patients did not come under observation until later childhood. The first symptoms to be noted are pallor, enlargement of the abdomen, a yellowish tinge of the skin and weakness. Splenomegaly is a constant finding and occurred to a slight degree even in the cases that were observed early. With time these early symptoms become more pronounced, and in addition anorexia, fever and edema may develop. Later the spleen is greatly enlarged and the liver is moderately hypertrophied. Varying degrees of jaundice are present in most of the cases presented, but this may be slight or absent at times throughout the course.

In the beginning, the roentgenographic findings are not distinctive. After the symptoms have become definitely established, all of the long bones show a porous appearance with sharp trabeculations and thinning of the cortex. The flat bones of the skull show medullary thickening and radial striations, while the tables are usually thin. The typical mongoloid features due to widening of the cranial and the malar bones commonly occur after the disease has become well established. One of Cooley's cases did not show this characteristic, but the condition was apparently in an early stage.

Examination of the blood reveals a low hemoglobin and erythrocyte count. There are considerable anisocytosis and poikilocytosis. Reticulocytes and normoblasts are increased. The fragility of the red blood cells is normal or slightly decreased. The leukocyte count may be normal or increased. The differential count is but slightly altered, although young myeloid or lymphoid cells are frequently seen. Evidence of increased hemolysis is quite constant, as demonstrated by the high values for the icterus index, the positive indirect van den Bergh reactions and large amounts of urobilinogen in the stools and urine.

The response to therapy is not encouraging. Small, frequent transfusions of blood combined with careful diet and hygienic measures fail

to produce lasting beneficial results. Splenectomy is not followed by improvement, as is observed in cases of familial icterus. Stillman [7] and later Cooley [2] noted that following splenectomy there is a definite and prolonged increase in the number of nucleated red blood cells. Wollstein and Kreidel [6] drew particular attention to this finding as an aid in the differential diagnosis between this form of anemia and hemolytic icterus.

The course of the disease is slowly and progressively fatal. In reviewing the summary of the cases (table), the shortest duration was found in case 19 (S. S.) here reported, in which the patient died at 17 months of age. The patient whose case was reported by Hitzrot, on the other hand, was alive and quite well ten years after the onset of the disease. Of the twenty-three cases, seven terminated fatally, and none of the remaining sixteen patients was reported as definitely recovered when last observed.

REPORT OF CASES

CASE 1.—*History.*—S. S., a girl, aged 3 months, was admitted to the hospital on Feb. 11, 1930, because of increasing pallor and yellowness of the skin. The parents were born in Italy and were well. There were three other sisters and one brother in the family, and all were in good health. The mother had had no miscarriages. Eighteen years had elapsed since the last pregnancy. The patient was delivered at home by a midwife. The delivery was apparently without complications, and the weight at birth was about average. The mother had an adequate supply of breast milk, and the patient had gained steadily since birth. No cod liver oil or orange juice had been given. The mother had noticed that the infant had been getting pale since 2 months of age.

Examination.—The baby was well developed and of normal weight for her height and age, but was anemic and slightly jaundiced. Mongoloid features were not noted, and the size and shape of the head were not unusual. The anterior fontanel measured 2 by 2.5 cm. The general musculature was good, and there was no evidence of rickets. No enlargement of the lymph glands was noted. A soft systolic murmur was heard at the apex of the heart. The spleen and liver were both moderately enlarged.

The hemoglobin (Sahli) was 20 per cent. The bleeding time, coagulation time and platelet counts were normal. A direct transfusion of blood was given on admission before complete studies of the blood were made.

Course.—Following the first transfusion the hemoglobin rose to 66 per cent and the red cells to 4,000,000. The white blood cells numbered 34,000, with polymorphonuclears, 19 per cent; lymphocytes, 80 per cent, and eosinophils, 1 per cent. There were 9 nucleated red blood cells per hundred leukocytes. Anisocytosis and poikilocytosis were marked. Resistance to salt solutions was normal; hemolysis began at 0.40 per cent and was complete at 0.28 per cent. The results of the intradermal tuberculin test and the Wassermann reactions of the blood were negative. On the day following admission another transfusion of blood was given, followed by a rise in hemoglobin to 88 per cent. A solution of iron and copper was administered in large amounts, and no other therapy was instituted. The mother continued to nurse the baby. The patient was observed for two weeks in the hospital,

during which time the hemoglobin continued to increase, with a slight rise in the polymorphonuclear cells. She was sent home with a regulated diet containing viosterol, cod liver oil and orange juice.

Two months later, on April 15, at the age of 5 months, the patient was readmitted to the hospital. The hemoglobin had fallen to 36 per cent and the red blood cells to 3,200,000. The white blood cells numbered 24,200, with polymorphonuclears, 48 per cent; lymphocytes, 41 per cent, and eosinophils, 11 per cent. Punctate basophilia was marked, 24 per hundred white blood cells. Normoblasts numbered 18 per cent. Reticulation was increased to 18.2 per cent. The blood calcium was 10.8 mg. and the phosphorus was 6 mg. Fragility began at 0.44 per cent and

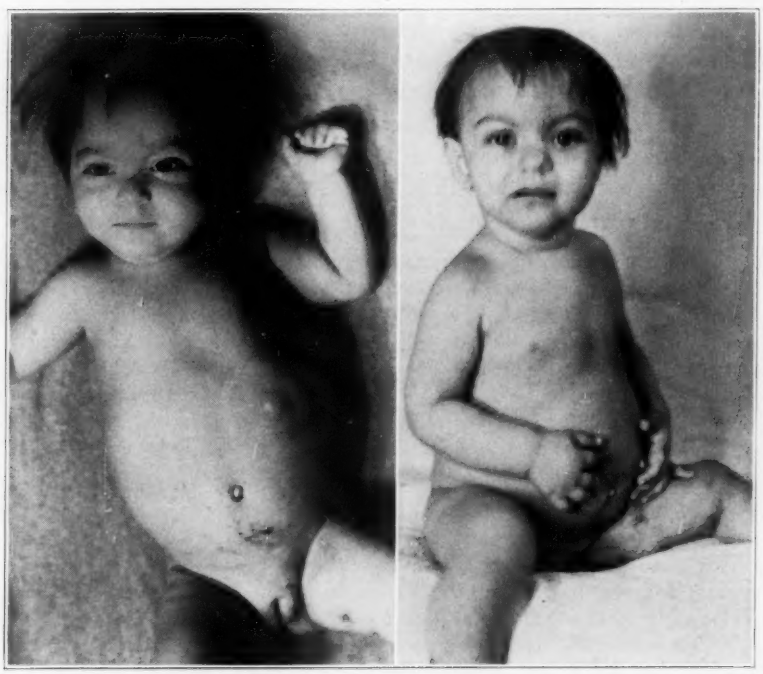


Fig. 1 (case 1).—The appearance of the patient at 6 and 14 months of age. Note the widening of the facies and the enlargement of the abdomen at 14 months.

ended at 0.28 per cent. Stool cultures were negative for ova and parasites, and blood cultures were sterile. Analysis of the maternal milk revealed all constituents in their normal proportions. The urine was normal. The patient's Wassermann reaction of the blood was again found to be negative, as were those of her parents.

At this time there was no evidence of jaundice or mongoloid features, but the head seemed to be unusually firm and a bony enlargement was noted in the median portion of the frontal bone. Roentgenograms of the long bones and skull showed no abnormalities. The spleen and liver were not appreciably larger than on the previous admission. The patient was given two transfusions of blood at weekly intervals followed by a gain in the hemoglobin content and number of red blood cells. She was observed at this time for three weeks. Artificial feeding was sub-

stituted for maternal milk. Saccharated ferrous carbonate, 30 grains (1.95 Gm.) daily, and liver extract were given and were continued at the time of discharge to the clinic.

The patient was again admitted to the hospital on June 23, at the age of 7 months. While at home she had been quite well until one week before entrance, when she became pale, refused to eat and was feverish. Study of the blood revealed: hemoglobin, 24 per cent; red cells, 2,750,000; white cells, 48,000, with polymorphonuclears, 30 per cent, and lymphocytes, 58 per cent. Punctate basophilia was marked; the normoblasts were 37 per cent. The reticulate cells were increased to 16 per cent. The platelets numbered 150,000. The blood calcium was 9.5 mg., and the phosphorus, 4.4 mg. Fragility again was noted to be normal. The icterus index was 12.2, and the van den Bergh reaction was positive in the indirect phase. At this admission 0.1 mg. of avian tuberculin was injected intracutaneously without a resultant reaction. Urobilinogen was found in the urine and stool on three occasions. No free hydrochloric acid was present in the contents of the stomach.

After an initial transfusion of blood, saccharated ferrous carbonate, liver extract, beef blood, fresh liver and an abundance of green vegetables constituted the therapy.

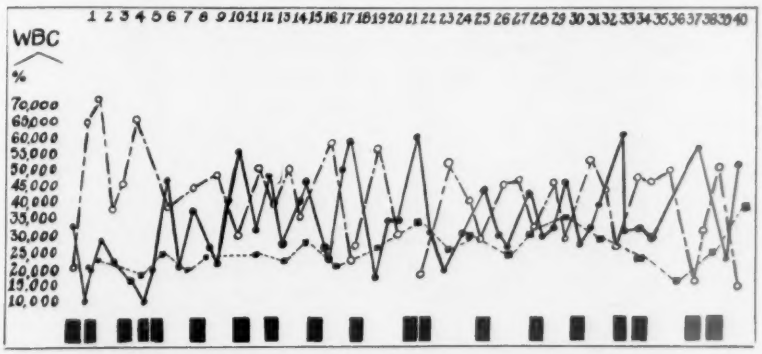


Fig. 2 (case 1).—The weekly fluctuations in the hemoglobin, white blood cells and normoblasts and their temporary response to transfusions of blood. The black circles indicate white blood cells; the white circles, hemoglobin; the black squares, normoblasts, and the black rectangles, transfusions.

This was continued for one month, during which time the hemoglobin gradually fell to 28 per cent, and another transfusion of blood was given. Further treatment included roentgen exposure over the long bones and the spleen, hydrochloric acid and ventriculin by mouth, and although no evidence of malarial organisms could be found, quinine was given. During this admission a course of antisyphilitic treatment was administered, and the Wassermann reaction was again found to be negative.

The failure to respond to general therapy is indicated in figure 2, which shows the numerous transfusions of blood that were necessary to prevent the development of the extreme anemia that was invariably accompanied by anorexia, irritability, fever and edema.

Roentgenograms taken on June 25, at the age of 7 months, revealed definite osteoporosis of all the long bones and some thickening of the frontal and occipital bones. A suggestion of mongoloid features now began to appear. These changes were more marked at the age of 1 year.

On April 16, at the age of 17 months, the patient was discharged to be observed at home. After a period of three weeks she was readmitted because of increasing pallor. Two transfusions of blood were administered, and she was again discharged.

The final admission was three weeks later. The hemoglobin was 18 per cent, and the red blood cells numbered 1,060,000. The white blood cells numbered 50,000, of which 24 per cent were polymorphonuclear cells, 28 per cent lymphocytes, 2 per cent eosinophils, 1 per cent basophils, 43 per cent nuclear shadows and 2

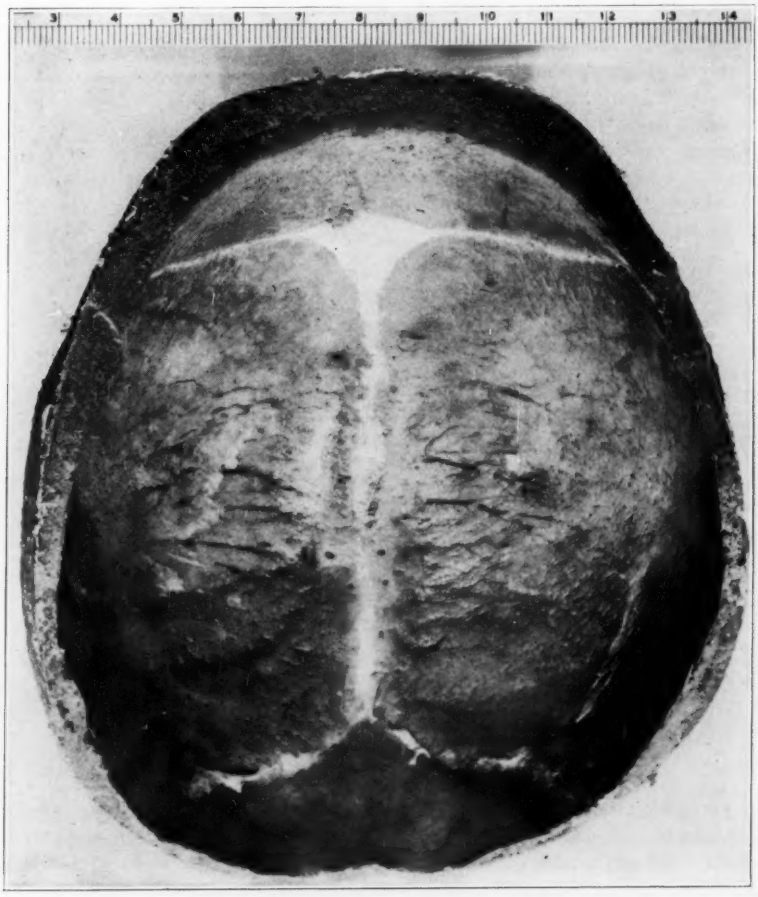


Fig. 3 (case 1).—The calvarium. Note the thickened frontal and parietal bones.

per cent myelocytes. There were 32 per cent normoblasts, and marked anisocytosis, poikilocytosis, basophilic stippling and polychromasia were present. The platelets numbered 80,000. While preparations were being made for a transfusion of blood, the patient suddenly died.

Postmortem Examination (Dr. J. Arnold de Veer).—The important observations were as follows: The body was that of a female infant about 18 months of age. The skin over the entire body was pallid, and the conjunctivae and the nasal and buccal membranes were anemic.

The lower margin of the liver extended to the right iliac crest. The liver weighed 680 Gm.; the surfaces were smooth, and the capsule was not thickened. The cut surfaces were not unusual except that the color was more golden brown than normal. The lower border of the spleen was at the left iliac crest. The weight of the spleen was 200 Gm. The anterior margin was rounded and presented several deep notches. The capsule was slightly thickened, and the outer surface was coarsely granular. The splenic tissue was firm in consistency and on section was a deep red. The malpighian corpuscles were indistinct, and a moderate amount of fibrous tissue could be distinguished throughout the organ. Both suprarenals were thinner than normal, particularly the left.

When the scalp was reflected, the cranial bones presented an unusual appearance. The frontal area was prominent. The surface of the bones was a dull, purplish red, which suggested a thin outer table. The surface was somewhat irregular, as though new bone had been laid down at various points. The calvarium was found to be unusually thick, particularly in the frontal and parietal regions. The cut edge of the bones showed a uniform purplish-red color. The bone was uniform in consistency and could easily be cut with a knife. The usual division into inner and outer tables with diploe between was entirely lacking. The brain and its coverings were grossly normal. When the dura was stripped from the base of the skull, the same purplish-red color was observed. The orbital portions of the frontal bones were unusually prominent, which suggested marked thickening.

The right femur and humerus were removed for examination and were normal in shape and outline, but the cortices were unusually thin, revealing in some areas the underlying marrow.

Microscopic Examination.—Sections through the liver, pancreas, thymus, lymph nodes and periosteum gave a strongly positive reaction for iron when stained by potassium ferrocyanide and hydrochloric acid.

The thymus presented the appearance of the involuting organ of late adolescence. Fully half of the gland was made up of loose connective and adipose tissue. In this stroma were set atrophic lobules of parenchymatous tissue. Hassall's corpuscles were almost entirely absent. When one was found it was apt to be very small and difficult to identify with certainty.

The suprarenals were unusually thin. The cortical substance and a few small areas of medullary tissue appeared normal. There was an apparent relative decrease in the medullary portion.

The thyroid tissue was edematous. The acini of the glands for the most part were poorly formed and contained little or no colloid. Frequently the cells occurred in clusters with no acinar arrangement.

Little of the normal architecture of the spleen remained. No malpighian bodies could be found. The splenic pulp was moderately fibrotic and through it coursed numerous wide sinusoids. Throughout the pulp were found myeloid and lymphoid cells in about equal proportions. A good many polymorphonuclears and forms resembling myeloblasts and myelocytes were found. An occasional megakaryocyte was also seen. These cells were found lining the sinusoids, where they appeared as an irregular fringe, obscuring the endothelial lining cells. Some of the sinusoids were densely filled with these cells.

One of the enlarged retroperitoneal lymph nodes showed essentially normal architecture, with the numerous germinal centers well retained. Throughout the pulp, however, in addition to numerous lymphocytes, were found many myeloid cells resembling those seen in the spleen. Near the capsule of the node were dense collections of large phagocyte cells laden with hemosiderin.

The bone marrow from the ribs, ileum and the body of one of the vertebrae showed essentially the same picture. The bony trabeculae were almost uniformly distorted throughout the bone. No cortical condensation was found. All of the specimens contained very cellular marrow which in places was found directly beneath the periosteal covering of the bone. Evidence of hematopoiesis was entirely lacking. Leukoblastic cells comprising almost the entire marrow were seen. Here, as in the spleen, were large hemosiderin-laden phagocytic cells, which were particularly numerous just beneath the periosteum. There was evidence of a simultaneous distortion of bone and new bone formation. Beneath the periosteum was a considerable amount of osteoid tissue.

Fig. 4 (case 2).—The appearance of the patient at 8 years of age. The mongoloid facies is pronounced.

CASE 2.—*History.*—R. R., an Italian boy, aged 8 years, was admitted to the hospital on Nov. 14, 1930, with the complaints of yellowness of the skin and enlargement of the head. There were eight children in the family, and all were said to be living and well. However, on later examination, a younger sister (case 3 here reported) was found to have anemia, splenomegaly and characteristic roentgenographic changes in the bones. The patient's birth history was quite normal, but the parents noted soon afterward that he was quite pale. This pallor was marked at 1 year of age, when they noted enlargement of the head and a yellow discoloration of the skin. He was not examined until he was 5 years of age, when admitted

to St. Catherine's Hospital, Brooklyn, because of fever and marked edema of the lips and face. He was observed for two months and was found to have a hemoglobin of 41 per cent; the red blood cells numbered 2,350,000; the white blood cells, 6,000, with 76 per cent polymorphonuclear cells, 14 per cent small lymphocytes, 1 per cent basophils and 9 per cent large lymphocytes. There were 16 per cent

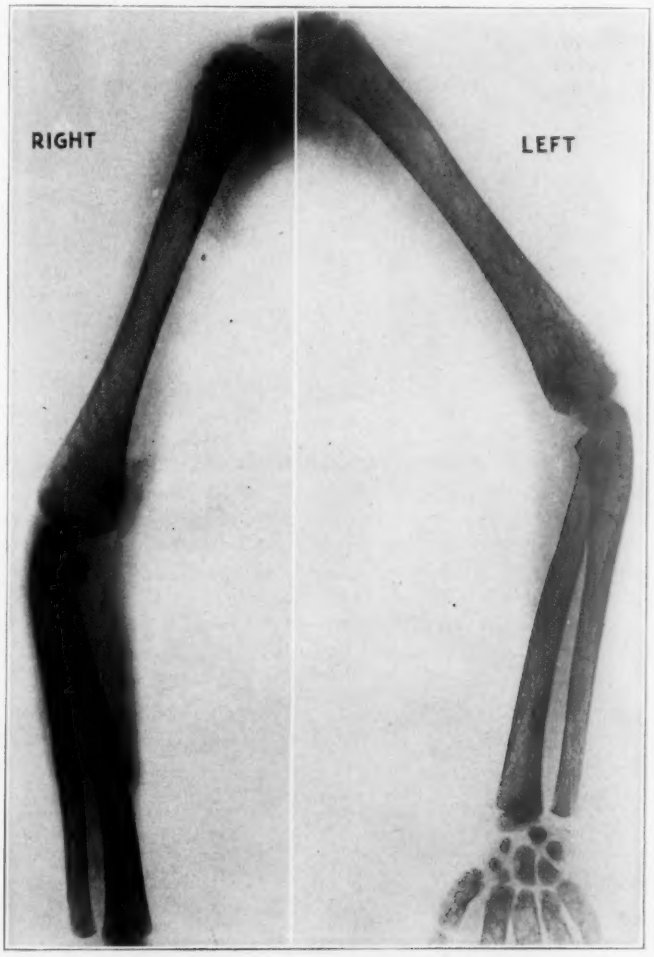


Fig. 5 (case 2).—The upper extremities, showing the porosity of the long bones.

nucleated red cells. The icterus index was 20, and the van den Bergh reaction was positive in the indirect phase. The fragility of the red cells was slightly decreased. The platelet count was 240,000. The Wassermann reaction of the blood was negative. At this examination the spleen was four fingerbreadths below the left costal margin. Fluoroscopic examination revealed a marked degree of skeletal porosity. The head was noted to be enlarged, and the features were definitely mongoloid, but roentgenographic examination of the head was not made.

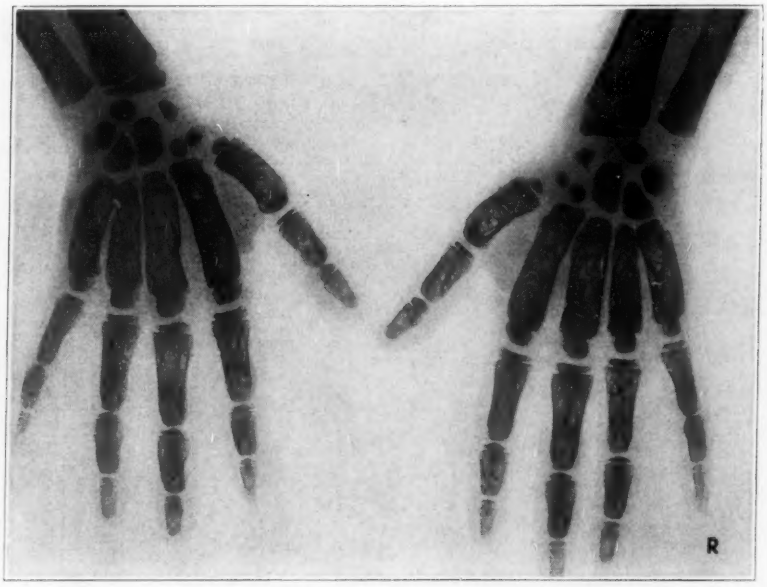


Fig. 6 (case 2).—Roentgenogram, showing the extreme porosity of the bones of the hands.

Fig. 7 (case 2).—The appearance of the skull at the age of 8 years.

During the next three years, the boy was quite active at home, but did not attend school because of his appearance. He was not observed again by a physician until the day of admission to the Long Island College Hospital.

Examination.—On admission to the hospital, the patient was noted to be jaundiced, and malnutrition was extreme. The head measured 59 cm.; the malar bones were wide and prominent. A soft systolic murmur was heard over the apex. The lower border of the spleen was at the iliac crest, and the liver was enlarged 8 cm. below the right costal border.

Examination of the Blood.—The hemoglobin was 38 per cent, and the red blood cells numbered 2,100,000. There were 13,100 white blood cells, with polymorphonuclear cells, 56 per cent; lymphocytes, 37 per cent; eosinophils, 5 per cent, and transitionals, 2 per cent. The normoblasts numbered 21 per cent. Anisocytosis and poikilocytosis were marked. There was considerable basophilic stippling. The platelets numbered 210,000, and the bleeding and coagulation times were within normal limits. The icterus index was 18.3, and the van den Bergh reaction was positive in the indirect phase. The fragility of the red cells was normal. The Wassermann reaction was negative. The blood calcium was 9.4 mg., and the phosphorus was 5.7 mg.

There was no free hydrochloric acid in the contents of the stomach. Urinalysis gave negative results. Urobilinogen was increased in both the urine and the stools. The Bence-Jones test gave negative results. Parasites were not found in either the blood or the stools.

Roentgenologic Studies (Dr. A. L. L. Bell).—Roentgenographic examination of the long bones revealed unusual thinning and porosity of the cortices. The medullary cavities, especially at the extremities of the shafts, showed numerous rounded areas of decreased density, giving vacuolated appearances to the bones. These findings were also present in the carpals, metacarpals, tarsals and phalanges.

The cranial bones were unusually thick, particularly the frontal and anterior two thirds of the parietal bones. The inner table was intact and somewhat increased in density. The outer table could not be seen except at one point in the posterior portion of the frontal region. The cancellous portions of the bones involved were markedly thickened and showed radial striations throughout.

Course.—The patient was observed for three months in the hospital, during which time his general condition remained unchanged. Therapy consisted of frequent transfusions of blood and general treatment directed toward hematopoietic stimulation. He is being observed at frequent intervals in the outpatient service, and the anemia and weakness are gradually progressing.

CASE 3.—*History.*—M. R., aged 5 years, is a sister of R. R. (case 2). This child was found to present the same clinical features as her brother. It is interesting to note that another brother chronologically between the patients in cases 2 and 3 was found to be normal. After the mother's attention had been directed to this child, she recalled that her skin had gradually been assuming a yellowish muddy color and that her head had been growing larger. The past history was otherwise irrelevant.

Examination.—On admission to the clinic, the child evidenced a slight yellow tint to the skin and sclerae, enlargement of the head and widening of the facial bones. The spleen was 3 cm. below the left costal margin, and the liver was but slightly palpable. No evidence of infection was noted.

Examination of the Blood.—The hemoglobin was 50 per cent, and the red blood cells numbered 2,900,000. The white blood cells numbered 9,300, with 57 per cent polymorphonuclears, 39 per cent lymphocytes, 2 per cent eosinophils, 1 per cent

transitionals and 1 per cent myelocytes. The normoblasts numbered 8 per cent. The platelet count was 240,000, and the bleeding and coagulation times were normal. The icterus index was 8.8, and the van den Bergh reaction was faintly positive in the indirect phase. Fragility of the red cells was within normal limits. The blood calcium and phosphorus were not decreased. The Wassermann reaction of the blood and the results of a tuberculin test were negative.

Urobilinogen was not increased in the urine. Parasites were not found in either the blood or the stools.

Roentgenograms of the skull and long bones revealed the characteristic findings as described in case 2, although the changes were more moderate. This patient is being treated in the outpatient department and shows no signs of improvement.

CASE 4.—*History.*—L. S., a boy, aged 10 months, was brought to the hospital on April 24, 1931, because of pallor and weakness of four months' duration. The parents were Italian. One other brother had died at the age of 2 years from an undiagnosed illness. The developmental history was normal, and the feeding history was unusually good. Every known method had been employed to combat the progressive anemia.

Examination.—The infant was well developed and well nourished, although quite pale. No evidence of rickets was noted. The head was definitely enlarged and was described as having a "stony feel." The anterior fontanel was closed. The bridge of the nose was depressed, and the malar bones were widened. The skin showed a muddy yellow discoloration, and a slight icteric tint was present in the sclerae. The edge of the liver was palpable 3 cm. below the costal margin, and the lower border of the spleen was felt 6 cm. below the costal border.

Examination of the Blood.—This revealed: red cells, 2,900,000; hemoglobin, 45 per cent; leukocytes, 15,000, with polymorphonuclear neutrophils, 38 per cent; lymphocytes, 57 per cent; eosinophils, 4 per cent; myelocytes, 1 per cent, and normoblasts, 10 per cent. Polychromasia, anisocytosis and poikilocytosis were marked. The platelets numbered 220,000. The bleeding and coagulation times and the clot retraction time were within normal limits. The fragility of the red blood cells was normal. The icterus index was 15, and the van den Bergh reaction was positive in the indirect phase. The Wassermann reaction was negative. The calcium and phosphorus were normal.

Urobilinogen was slightly increased in the stools and urine. The Pirquet test gave negative results.

Roentgenographic examination of the skull and long bones revealed the typical findings described in case 2, but to a lesser degree.

Course.—Two small, direct transfusions of blood were given soon after admission followed by a temporary increase in the hemoglobin. After discharge from the hospital, the patient required frequent transfusions to overcome the persistent anemia. Frequent infections had developed, and he was constantly under medical supervision.

CASE 5 (By courtesy of Dr. T. B. Givan, from his clinic at the Cumberland Hospital, Brooklyn).—*History.*—M. B., an Italian girl, aged 9 years, was admitted to the hospital because of pallor and weakness. An older sister, aged 10 years, had died of anemia and enlargement of the abdomen. Four younger children were living and healthy.

Examination.—The patient was quite active, although the pallor was extreme. Jaundice was evident, and her facies had a definite mongoloid appearance. The head was enlarged, measuring 51 cm. in circumference, and had the same stony

feel noted in the other cases. The heart and lungs were normal. The spleen was palpable 10 cm. below the costal border, and the liver was 4 cm. below the costal edge.

Examination of the Blood.—This revealed: hemoglobin, 45 per cent (Sahli); red cells, 2,390,000; white cells, 8,800, of which 44 per cent were polymorphonuclear cells, 50 per cent lymphocytes, 4 per cent eosinophils and 2 per cent transitionals. Anisocytosis, poikilocytosis and polychromasia were marked. The reticulocytes numbered 5.8 per cent, and the normoblasts, 16 per cent. The platelets numbered 225,000, and the bleeding and coagulation times were normal. Fragility of the red cells was normal. The values for the blood calcium and phosphorus were not decreased. The Wassermann reaction of the blood and the results of a tuberculin test were negative. The icterus index was 18.7, and the van den Bergh reaction was faintly positive in the indirect phase. Iso-agglutination was absent.

Fig. 8 (case 5).—The appearance of the skull at the age of 9 years.

Urobilinogen was increased in the urine and stools. Neither parasites nor ova were seen in the blood or stools.

Roentgenograms of the skull and long bones revealed the characteristic changes common to these cases, especially in the skull.

Course.—This patient was discharged from the hospital as unimproved, and was to be observed at regular intervals in the clinic.

COMMENT

It is certain that the changes in the bones associated with these cases are not new. Williams [12] has described pathologic changes in the skulls of pre-Columbian Peruvians and North American Indians which he observed and found to resemble the changes seen in hemolytic anemia.

12. Williams, H. U.: Human Paleopathology, with Some Original Observations on Symmetrical Osteoporosis of Skulls, Arch. Path. **7**:839 (May) 1929.

Hutchison,[13] in his Gaulstonian lectures, while discussing splenic anemia, described an enlargement of the frontal and parietal bones which he attributed to rickets. Gänsslen,[14] describing cases of familial hemolytic icterus, called attention to the peculiar facies and the tower-shaped skulls in some of his cases. Neither Hutchison nor Gänsslen studied these findings by roentgenograms or at autopsy.

There is a possibility that some of the cases first described by von Jaksch,[3] Hayem [15] and Luzet [16] and many subsequent cases later diagnosed as von Jaksch's disease with rickets may have had changes in the bones. The patient in case 1 in this report was observed throughout her entire illness, and in the beginning there was little to indicate the future course other than the grave anemia. However, after observing the progress and later enlargement of the cranial bosses with no demonstrable evidence of rickets, the type of anemia described by Cooley was considered. Roentgenograms of the skull and bones gradually became more characteristic, until finally the case was typical.

It is interesting to observe in case 1 that in spite of the severe and progressive anemia, no extrahematopoietic centers as described by Brannan [17] were found at autopsy, although cross-sections through the calvarium revealed the frontal areas to be dark red, soft and easily cut with a knife. The elevations involved only the outer table and diploe as he described.

SUMMARY

Erythroblastic anemia should be considered as a definite disease entity. It is a grave and chronic anemia with familial and racial tendencies. Chronic infections, rickets and other nutritional disorders are of no etiologic importance. The onset is in early infancy and is accompanied by splenomegaly and some degree of icteric discoloration of the skin. There may be progressive enlargement of the cranial and malar bones with associated mongoloid facies. Studies of the blood frequently reveal, besides the low hemoglobin and the erythroblastosis, a leukocytosis of varying degree and often an increase of myeloid or

13. Hutchison, Robert: Some Disorders of the Blood and Blood-Forming Organs in Early Life, Lancet **1**:1323 (May 14) 1904.

14. Gänsslen, M.: Ueber hämolytischen Ikterus, Deutsches Arch. f. klin. Med. **140**:210 (Sept.) 1922. Gänsslen, M.; Zipperlen, E., and Schüz, E.: Die hämolytische Konstitution, ibid. **146**:1 (Jan.) 1925.

15. Hayem, Georges: Du sang et de ses altérations anatomiques, Paris, G. Masson, 1889.

16. Luzet, C.: Études sur les anémies de la première enfance et sur l'anémie infantile pseudo-leucémique, Thèse de Paris, 1891.

17. Brannan, Dorsey: Extramedullary Hematopoiesis in Anemias, Bull. Johns Hopkins Hosp. **41**:104, 1927.

lymphoid cells. There is evidence of increased hemolysis in the high icterus index and positive indirect van den Bergh reactions, although the fragility of the red cells is not increased. The course is not altered by any of the recognized forms of hematopoietic stimulation. The benefit of a transfusion of blood is but temporary. Following splenectomy, there is a marked and sustained increase in the circulating normoblasts, which is characteristic, but beneficial results are not observed.

Eighteen cases that have shown the changes in the bones have been summarized from the literature, and five additional cases have been reported.

Dr. C. H. Laws placed his departmental records at our disposal.

RACIAL OR FAMILIAL ANEMIA OF CHILDREN

ASSOCIATED WITH FUNDAMENTAL DISTURBANCES OF BONE AND PIGMENT METABOLISM (COOLEY-VON JAKSCH)

G. H. WHIPPLE, M.D.
AND
W. L. BRADFORD, M.D.
ROCHESTER, N. Y.

The statement that knowledge relating to this disease condition is in an unsatisfactory state will be accepted without argument. Many authors feel that von Jaksch did not describe this disease, and that the term "von Jaksch's anemia" includes a miscellaneous group of diseases. As described by Cooley [1] this disease now has a well established and cleancut clinical picture, with careful reports from a number of clinics in this country. Cooley [2] considered the condition as essentially due to hemolysis, and related the bone changes to the extreme hyperplasia of the red marrow. Wollstein and Kreidel [3] referred to the disease as a familial hemolytic anemia. It is fair to state that the study of anatomic material has not been as complete and satisfactory as the clinical reports. For this reason it seemed wise to report in detail the gross and histologic observations in the two cases herein reported.

Pigmentary abnormalities were studied with especial care, and in case 1 present some startling departures from normal. Pigmentary disturbance may be unusual in this case, but case 3 shows similar though early changes in the liver, and we are inclined to believe that similar pigmentary abnormalities will be found when careful studies are made of the viscera in other cases. Case 1 in which pigment deposits were found in the liver, pancreas, stomach, salivary and mucous glands, thyroid, parathyroids, suprarenals and pituitary reminds one of hemochromatosis.

The abnormalities of the bones do not appeal to us as being due simply to hyperplasia of the marrow. There is no change of this nature

---

From the Departments of Pathology and Pediatrics, University of Rochester School of Medicine and Dentistry.

1. Cooley, T. B.: von Jaksch's Anemia, Am. J. Dis. Child. **33**:786 (May) 1927.

2. Cooley, T. B.: Likenesses and Contrasts in the Hemolytic Anemias of Children, Am. J. Dis. Child. **36**:1257 (Dec.) 1928.

3. Wollstein, Martha; and Kreidel, K. V.: Familial Hemolytic Anemia of Childhood—von Jaksch, Am. J. Dis. Child. **39**:115 (Jan.) 1930.

in other anemias with hyperplasia or in experimental anemias with extreme hyperplasia. It suggests to us a metabolic disturbance that involves certain bones in a recognizable fashion with remarkable uniformity. In some respects the changes in the bones suggest scurvy and in other respects, abnormalities of the ductless glands. We prefer to think of these bony changes as due to some defect of metabolism either racial or associated with ductless gland imbalance or some other unknown factors. This point of view invites an entirely different approach to the study of this disease.

To formulate our belief as to the essential pathology of this disease is difficult and admittedly unsatisfactory, but it is somewhat as follows: The marrow picture is more like that of pernicious anemia, and therefore could be explained as due to the lack of something at present unknown. The pigment deposit (case 1) is extreme, but similar less conspicuous pigmentary abnormalities may be observed in other cases and, like hemochromatosis, suggest some fundamental lack or change in the normal method of handling pigment in the body. The changes in the bones suggest to us a disturbance of metabolism of a fundamental nature, like scurvy or acromegaly rather than an adaptive reaction to marrow hyperplasia. One may think of all three abnormalities as related and due to an inherited defect that causes this fundamental change in internal metabolism during growth. One may think of such perverted metabolism as capable of remedial adjustment when all the factors at present unknown are understood. One may be permitted to try various dietary factors and even gland therapy in an effort to solve the clinical problem by simple empiricism. Meanwhile a study of every factor of internal metabolism is highly desirable.

CLINICAL AND ANATOMIC DATA

The clinical material consists of observations made on three children, all of whom we believe may be classified, on the evidence presented, as having "erythroblastic anemia" as described by Cooley. All were of Italian parentage. Two of the patients (cases 1 and 2) were sister and brother, and both have died. Complete anatomic studies are presented for case 1. Though necropsy for case 2 was denied, the clinical evidence considerably strengthens the diagnosis for case 1. The third patient is still living at the time of writing and the clinical data represent a careful study of events from birth until this time (age 3 years). We are fortunate to have specimens of the liver and spleen from this child for histologic studies.

REPORT OF CASES

CASE 1.—*History.*—At the age of 2 years, C. G., an Italian girl, was noted to be pale and somewhat yellow. The parents were told that she suffered from anemia,

and she was treated with medicines, including cod liver oil, and exposure to sunshine under the supervision of her family physician. On June 14, 1930, she was seen in the office of another physician. At this time, the complaint was pallor and fatigue. Enlargement of the head and spleen was then noted. A healed fracture of the left leg was present. The clinical diagnosis of von Jaksch's anemia was made.

Course.—From June 17, 1930, until Jan. 2, 1931, she was observed by the staff of the Clifton Springs Sanitarium. She weighed 25½ pounds (11,550 Gm.) on June 18, 1930. Her weight gradually increased to 29¾ pounds (13,540 Gm.) on Nov. 3, 1930. At this time, edema of the face was noted, as well as a hematoma of the forehead. The general condition improved, but during the first week of January, 1931, a sudden relapse occurred, the edema and pallor becoming more pronounced.

TABLE 1.—*Observations on the Blood in Case 1* *

Date	Hemoglobin, per Cent	Red Blood Cells	White Blood Cells	Polymorphonuclears, per Cent	Myelocytes, per Cent	Lymphocytes, per Cent	Monocytes and Transitionals, per Cent
6/17/30	24	2,400,000	20,100	65.5	1.5	32.5	0.5
6/18/30	23	2,150,000	18,600	58.6	2.0	39.2	0.2
6/28/30	28	2,450,000	31,500	65.0	4.6	29.7	0.7
7/ 5/30	30	2,350,000	25,200	64.0	3.0	31.7	1.3
7/12/30	30	2,360,000	20,400	61.0	5.0	33.3	0.7
7/19/30	27	2,200,000	23,000	63.0	3.3	32.7	1.0
7/26/30	30	2,260,000	31,600	62.0	3.0	34.0	1.0
8/ 2/30	30	2,500,000	30,000	76.0	...	23.3	0.7
8/ 9/30	31	2,700,000	26,600	62.3	4.0	32.7	1.0
8/23/30	36	2,730,000	25,400	66.0	...	32.3	1.7
9/ 6/30	32	2,800,000	22,400	64.0	3.4	30.0	2.5
9/20/30	31	2,400,000	29,100	65.7	...	33.3	1.0
10/ 4/30	29	2,500,000	18,400	61.0	...	37.7	1.3
10/18/30	27	2,420,000	28,800	60.0	...	36.0	4.0
11/13/30	20	2,150,000	11,500	40.0	...	54.0	6.0
11/29/30	21	2,150,000	31,400	67.3	3.0	29.0	0.7
12/13/30	17	1,350,000	20,600	64.2	3.3	32.5	...
1/ 2/31	15	1,100,000	12,600	31.7	...	68.0	0.3

* Table 1 shows the typical blood counts in case 1 during the last six months of life. Obviously the white blood cell counts include nucleated red blood cells, which unfortunately were not enumerated. The terminal fall in hemoglobin and red blood cells is typical.

On January 7, at the age of 5 years, she was admitted to the Strong Memorial Hospital in a moribund state and died four minutes later, before a physical examination could be made.

Laboratory Data.—A sample of blood removed soon after death was subjected to the chemical studies, and the following results were obtained: The serum protein (refractometer method) was 9.33 per cent; the icterus index, 30 units, and the plant pigment, 0.013 mg. per hundred cubic centimeters (low).

Dr. S. A. Munford gave us the following records of blood counts and other laboratory data obtained during an observation of the patient at the Clifton Springs Sanitarium during the last six months of her life: On June 28, 1930, the icterus index was 30 units, and the van den Bergh test gave a positive reaction in ten minutes. A fragility test was made on July 6 with hypotonic salt solutions; hemolysis began at 0.38 per cent, and was complete at 0.32 per cent. Roentgenograms of the skull and the arms were made on June 21, 1930, and the following report was made: "The skull shows very marked thickening of the bone, and there is a very peculiar striated appearance seen in the bone. The bones of the arm show very marked thinning of the cortex and marked increase in the medul-

lary portion of the bone. There is also a rather peculiar mosaic appearance in the bones. These changes are found in the bones of patients suffering from von Jaksch's anemia."

A clinical report of case 1 and a brief anatomic review, together with excellent roentgenographic reproductions and photographs, were given by Dr. Munford.[4]

Autopsy.—Autopsy was performed by one of us (G. H. W.).

The anatomic diagnosis was anemia with hyperplasia of the marrow and abnormalities of the bones. There was pigmentation of the viscera and lymph glands. The liver and spleen were enlarged. Aplasia of the suprarenals, early bronchopneumonia and edema of the lungs and fatty degeneration of the liver and myocardium were noted.

The body was that of a poorly nourished girl 88 cm. in length. Rigor mortis was present; livor mortis was not obvious. The skin was somewhat darkly pigmented, but showed nothing unusual for an Italian child of the age of the patient. The head was large, and the features had a definite mongolian cast. The skull seemed to be rather square. The four upper front teeth were missing. The jaw was thickened, and the calvarium was greatly thickened, as found on incision, measuring in its thickest portion 1.8 cm. The subcutaneous fat had almost entirely disappeared. The muscles were very pale pink and poorly developed. The peritoneal cavity contained a little excess fluid which was a lemon yellow. The pleural cavities contained nothing unusual. The pericardial cavity contained 10 or 15 cc. of lemon yellow pale fluid. There were no adhesions in any of the serous cavities. The position of the organs was normal. The liver filled an unusually large portion of the upper part of the abdomen. The spleen was enlarged.

Heart: The heart weighed 155 Gm. The epicardium was smooth and glistening. The epicardial fat was scanty. The chambers of the heart contained rather soft but well formed postmortem clots. After twenty-four hours at room temperature or in the incubator blood clots showed no evidence of autolysis. The intima throughout was smooth. The tricuspid and pulmonary valves were normal. The mitral valve showed a few inconspicuous beads along the free margin, which were covered by endothelium and did not suggest an inflammatory process. The valve was normal and appeared competent. The aortic valve was normal. The heart muscle of the left ventricle was pale and distinctly mottled with yellow cross-striations, the typical appearance of myocardium associated with fatty degeneration. The myocardium, on section, was pale reddish brown and uniform in texture. The coronary vessels were normal. The heart muscle cells appeared normal. There was little pigment of any sort. In a few heart cells were seen small grains of yellow pigment, probably a lipochrome pigment, which did not stain for iron.

Lungs: The left lung weighed 150 Gm.; the right, 225 Gm. The lungs were identical in appearance. The pleural surfaces were smooth and looked marbled. Gray air-containing areas alternated with pink, rather heavy areas which contained less air. The glands at the hilus were enlarged and pigmented, as were others in the body. No coal pigment was noted. The bronchi showed a rather swollen, velvety, pink mucosa. Sections of the lungs were moist and showed the same mottling as that described for the surface. There were no distinct areas of consolidation, but some of the alveoli may have contained a few cells together with fluid. Beginning bronchopneumonia was suspected.

Some alveoli contained albuminous material with a few cells and very little fibrin. There were a few large phagocytes in the alveoli which contained a granular pigment giving a positive reaction for iron. There was a small amount of coal pigment. The mucosa of the bronchi showed a few fine grains of pigment at the

4. Munford, S. A.: Clifton M. Bull. **17**:107, 1931.

base of the epithelial cells. Some of this gave a positive reaction for iron. The cartilage was entirely normal, and showed no pigment. The large vessels were normal and showed no pigment in the smooth muscle. Mucus glands about the large bronchi contained many small granules of pigment which gave a strong positive reaction to the iron stain.

Spleen: The spleen weighed 105 Gm. It was regular in outline and decidedly firm and solid in texture. The cut surface was sharp, not velvety. The malpighian

Fig. 1 (case 1).—Photomicrograph of spleen, showing nests of foam cells in pulp and thickened sinusoids; magnification × 200.

bodies were unusually small for a child. The trabeculae were inconspicuous. The pulp was rather pale; it had a rusty tint, and was glassy and not increased in amount.

The spleen showed a diffuse increase in connective tissue, giving a considerable relative increase in the bulk of the spleen pulp as compared with the malpighian bodies, which were small but otherwise normal. The sinusoids of the spleen pulp were fairly conspicuous, easily made out and lined with well developed endothelium. The basement membrane seemed definitely thickened. The endothelium

contained abundant finely granular yellow pigment which gave no reaction for iron. In the spleen pulp there were large phagocytes, some of which contained a few granules of pigment which reacted with iron stains. In some areas there were considerable numbers of pale mononuclear cells of considerable size having a finely granular or frothy protoplasm and vesicular nuclei of rather small size. These may be designated as foam cells. Some of them contained a few granules of

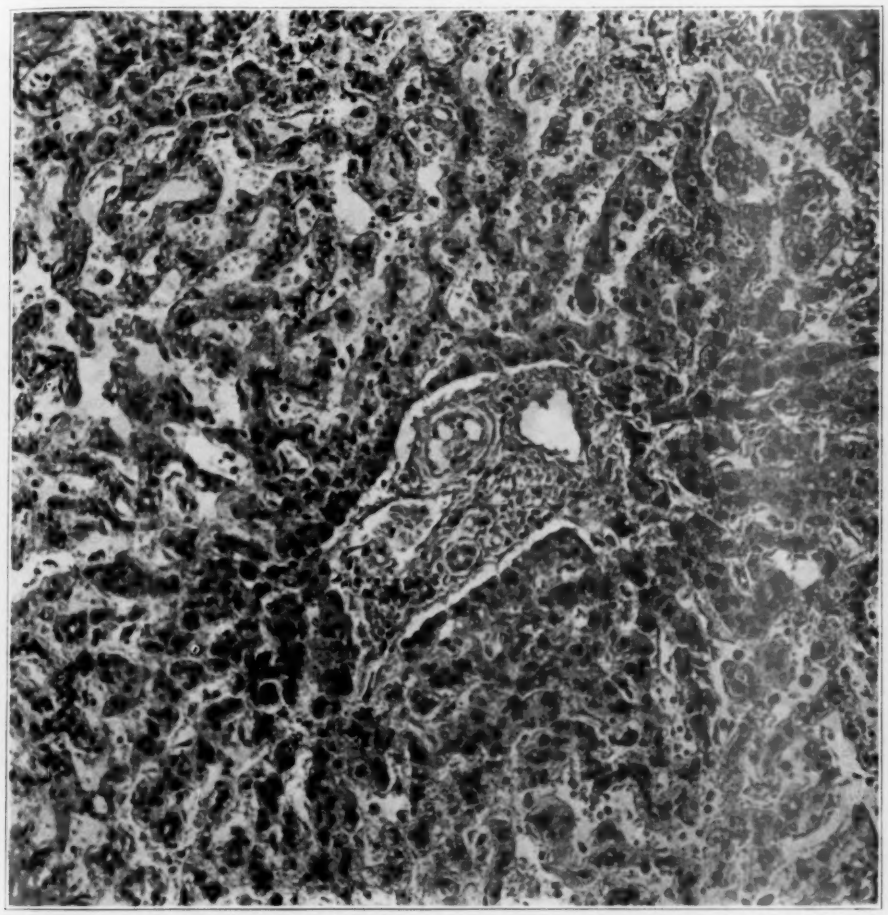


Fig. 2 (case 1).—Photomicrograph of lobules of the liver, showing much iron-staining pigment in the hepatic epithelium about the portal spaces; magnification × 175.

pigment which gave a positive stain for iron, but the majority of them showed no pigment (fig. 1). These cells did not give a positive reaction with stains for fat (sudan 3). They did not occur uniformly throughout the pulp but in islands as illustrated. They appeared to be some type of phagocyte as evidenced by occasional grains of pigment. Eosinophilic cells were fairly numerous, but no more so than in the submucosa of the intestine. They were scattered about in the spleen pulp, not occurring in islands or clumps. They were of all sizes and had nuclei

of every type. Some of them may have been myelocytes, but in the spleen there was very little evidence of its active participation in marrow activity with the formation of red and white cells. The presence of all the elements seen in the spleen pulp could be explained readily on the basis of filtration of the circulating blood and passive capture in the spleen pulp. A conspicuous feature in this spleen was the almost complete absence of pigment giving a positive stain for iron, which was in striking contrast with the findings in some of the other viscera and differed conspicuously from the findings in the usual forms of secondary anemia with destruction of blood. This suggests abnormal function.

Liver: The liver weighed 860 Gm. It was decidedly enlarged, and had a most unusual appearance, presenting a dull chocolate reddish-brown color. Lobulation was conspicuous through the thin capsule. On section the lobulation was seen to be quite regular. The border structures (Glisson's capsule) were not unusually thickened. There was a marginal brown zone about the portal spaces, and the centers of the liver lobules presented a yellow color (fatty degeneration). There was no evidence of necrosis. The gallbladder contained a little pale bile, and appeared to be normal.

The epithelium of the small and large ducts in the liver and of the gallbladder showed no abnormal pigment and appeared normal. The liver cells in the peripheral half of the lobule about the portal structures showed a rich pigment deposit within the epithelium. It consisted of a finely granular yellow pigment giving a strong reaction for iron (fig. 2). Otherwise the epithelium appeared relatively normal. The liver cells in the central half of each lobule showed distinct fatty degeneration, with fat droplets occupying more than half the bulk of the cell. This fat stained with sudan 3. These liver cells contained a finely granular yellow pigment in moderate amounts, but it did not give a positive stain for iron. The Kupffer cells contained a somewhat coarser yellow granular pigment which was highly refractile and did not give the slightest reaction to iron stains. This conspicuous difference between the pigment in various parts of the lobule and in the Kupffer cells was the most interesting feature of this organ.

Gastro-Intestinal Tract: The submaxillary gland showed a definite yellowish-brown pigmentation somewhat like that observed in the pancreas described below but of lesser intensity. The architecture was regular.

Both serous and mucous acini of the gland showed finely granular yellow pigment within the epithelium. Much of this gave a positive stain for iron. In general, the picture resembled that described for the pancreas, only the amount of pigment was a fraction of that found in the pancreas.

Tonsils: These were distinctly enlarged but not pigmented in contrast to the cervical lymph glands. Other structures of the throat and pharynx were normal.

The transitional epithelium covering the tonsil and its crypts showed no pigment. In general, the tonsil showed hyperplasia and nothing abnormal except in the very margins of the tonsillar tissue where the reticular cells and large phagocytes contained a few grains of pigment which gave a positive test for iron. This was in striking contrast to the cervical glands, which contained large amounts of pigment of several sorts. The mucus glands in the region of the tonsil showed a picture practically identical with that described in the mucus glands of the bronchi. They showed a rich deposit of finely granular pigment within the protoplasm of the gland epithelium which gave a positive reaction for iron.

The esophagus was normal. The stomach presented an unusual pigmentation of its mucosa, which was a dull, rusty brown. The mucosa appeared normal otherwise. The muscle coats did not appear to be pigmented.

The general architecture of the gastric mucosa was regular, and there was no evidence of chronic inflammation. The epithelial cells of the crypts were obviously full of granular pigment, which gave a strong positive test for iron (fig. 3). It was noted that this pigment was much more conspicuous in the lower half of the mucosa within the secretory epithelium, and it was abundant within the "chief cells" or cells having a basophilic stain, whereas the pigment was scanty in the "acid cells" within these same tubules. No degeneration of this epithelium was apparent. No pigment was noted in the submucosa and the muscle coats.

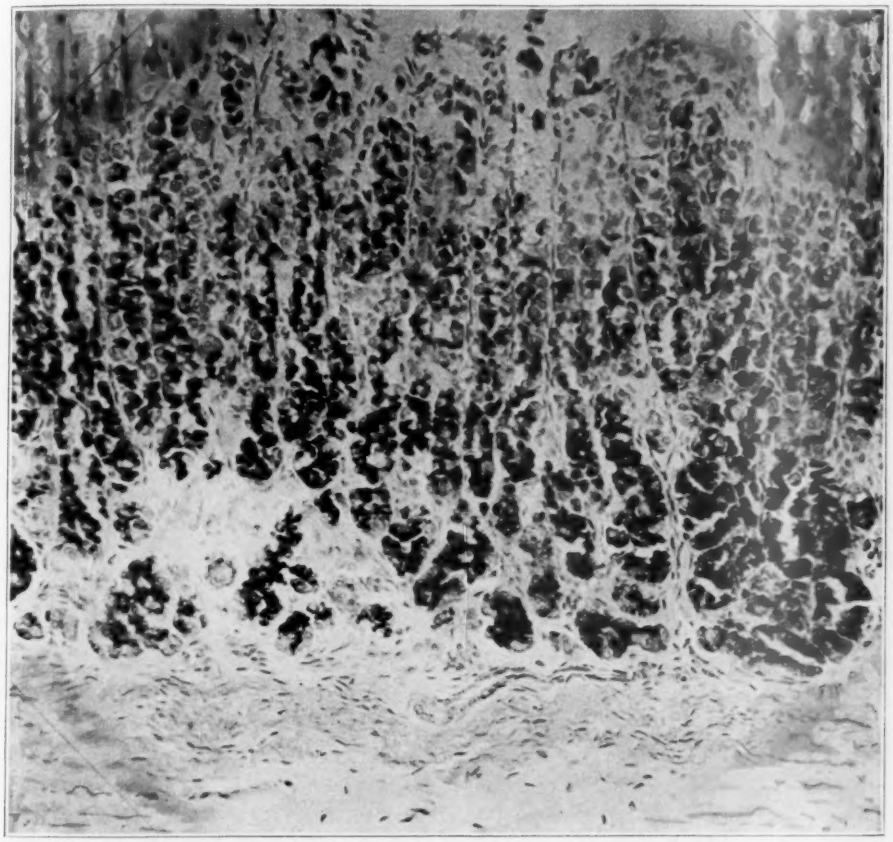


Fig. 3 (case 1).—Photomicrograph of gastric mucosa, showing iron-staining pigment in epithelium of tubules in lower half of mucosa; magnification × 175.

The duodenum contained bile. The mucosa was not pigmented.

The mucosa, in contrast to that of the stomach, contained no pigment in the mucosa or submucosa. Brunner's glands, however, just beneath the muscularis mucosae contained considerable finely granular yellow pigment in the epithelium of its acini. This pigment gave a positive test for iron. It had a definite tendency to deposit in the inner half of the cell adjacent to the lumen. The large vessels and muscle coats of duodenum were normal.

The jejunum showed a pale normal mucosa. In the ileum Peyer's patches were slightly pigmented, having a rather slaty cast. They were not enlarged. The solitary follicles were easily seen. The appendix was normal. The large intestine showed no pigmentation of its mucosa. The solitary follicles were fairly conspicuous but not enlarged.

The jejunum and ileum also showed absence of pigmentation in the mucosa and submucosa. There were numerous eosinophilic cells in the interglandular tissue.

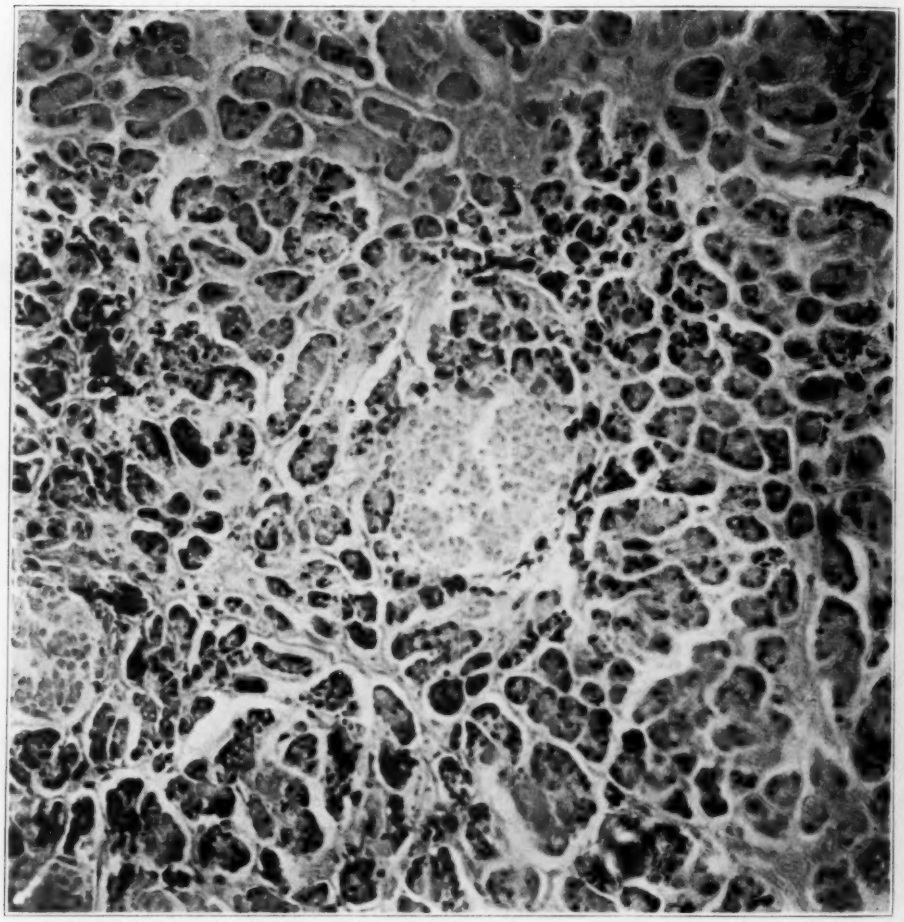


Fig. 4 (case 1).—Photomicrograph of pancreas, showing much iron-staining pigment in the epithelium of the acini and little pigment in the islands; magnification × 175.

Solitary lymph follicles in the region of the small intestine presented no pigment. Peyer's patches were noted in gross as slightly slaty tinted, but histologically there was no evidence of pigment. These structures appeared to be normal.

Pancreas: The pancreas presented an unusual pigmentation. It had a deep maple sugar or buff color, suggesting that of the pancreas in hemochromatosis.

Lobulation was regular, and the organ did not seem to be unusual, except for the pigmentation.

The remarkable pigmentation of the pancreas was due to a heavy deposit of granular pigment within the epithelium of the acini. This pigment gave a strongly positive test for iron (fig. 4). This pigment was deposited within the protoplasm of the cell, never in the nuclei. In some instances it increased to such an extent

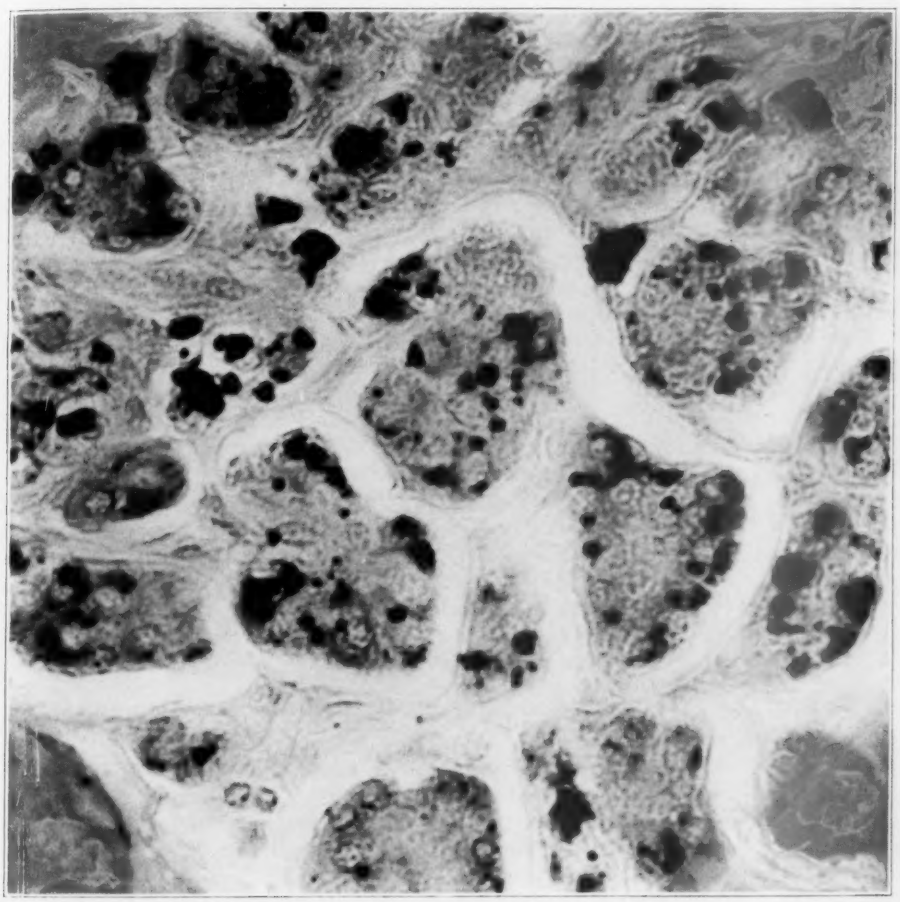


Fig. 5 (case 1).—Photomicrograph of section of pancreas, showing abundant iron-staining pigment in the epithelium of acini and occasionally in the phagocytes; magnification × 745.

that there was obvious degeneration of the cell, and therefore some of the pigment appeared within large phagocytes, although this change was not diffuse or conspicuous (fig. 5). The slight amount of increase of connective tissue may have been due to a deposit of pigment. The islands of Langerhans, in contrast with the acini, contained very small amounts of pigment, but they were definitely pigmented, particularly in the marginal portion. This pigment also gave a strong reaction for iron. It was noted that some acini contained pigment that did not stain for iron,

and others were completely free from pigment (fig. 5). The duct epithelium within the pancreas showed no pigment and was normal.

Kidneys: The left kidney weighed 110 Gm.; the right, 90 Gm. These organs were enlarged. The capsule came off, leaving a perfectly smooth, pale surface which showed the color often noted in pernicious anemia, a pale yellow brown. The glomeruli contained blood. The striations were normal. The cortex was about 5 mm. in thickness. The pyramids and pelves were normal.

The glomeruli appeared normal. Some of the convoluted tubules and loops of Henle contained a good deal of yellow granular pigment some of which stained for iron, but much of which did not. The majority of the tubules presented an appearance which was normal and free from pigment. In the pyramids the collecting tubules showed considerable amounts of very finely granular, highly refractile yellow pigment. This pigment did not give the slightest indication of an iron stain. There was no evidence that the epithelium was undergoing degeneration because of the presence of this pigment. The interstitial tissue and the blood vessels were normal. The amount of yellow granular pigment negative for iron exceeded many times that of the pigment giving a positive test for iron.

Pelvic Organs: The bladder contained a large amount of clear, lemon yellow urine. The mucosa was milky white. There was no pigmentation. The tubes, ovaries, uterus, vagina and rectum were normal except for evidence of anemia. Urine in the bladder gave a strong reaction for urobilin but a negative reaction for bile pigment.

There was no evidence of pigmentation or other abnormalities in the ovaries.

Lymph Glands: All the glands were enlarged, including the cervical glands, all the glands about the hili of both lungs and the glands of the mediastinum, retroperitoneum, pelvic region and mesentery, and particularly those in the gastrohepatic omentum. The last-mentioned glands measured from 1 to 2 cm. in diameter; the medulla was a deep chocolate and the cortex a pale gray. They were moist. They did not appear to contain blood. The mesenteric, retroperitoneal and pelvic glands contained a similar type of pigment but not in such great amounts, giving them a much paler color, but there was a definite chocolate-brown tint. Some of the glands in the neck contained blood and appeared like hemolymphatic glands; others showed some of this chocolate pigmentation. The bronchial glands were also enlarged and contained pigment. The glands back of the sternum likewise showed the same picture.

Almost all of the lymphatic tissue except the tonsils, solitary follicles, Peyer's patches and small lymph glands close to the mesentery showed more or less pigment. The picture in general in these tissues was similar, except for the extent of the deposit of pigment. The most heavily pigmented glands were in the gastrohepatic omentum and about the region of the pancreas. These glands showed definite edema but relatively normal lymph cords and germinal centers that were relatively free from pigment. The pigment obviously had been brought to the glands from elsewhere, and they acted as passive containers. Therefore, the greatest part of the pigment was in the peripheral sinus of the glands and in the medulla. In the peripheral sinus the pigment was granular but showed considerable variety in size. It was usually contained in large phagocytes. Some of it gave a positive stain for iron; some gave a definite stain for hemofuscin, and some gave no definite stain for either pigment. The pigment in the medulla of the gland was rather more coarsely granular and definitely more refractile, having a bright yellow color and giving no reaction for iron or hemofuscin. Some of this pigment was deposited within the reticulum of the gland structures, and much of it was found in phagocytes. The upper mesenteric and retroperitoneal glands

were heavily pigmented, as previously described. In some of the larger glands were large pale phagocytes having relatively small vesicular nuclei and a pale granular or frothy protoplasm; they may be designated as foam cells. They closely resembled similar cells described in the spleen and marrow. Some of them contained a little pigment and others did not. The bronchial lymph glands contained a little coal pigment and small amounts of pigment similar to that described. The cervical glands contained only a moderate amount of pigment as described. It would appear that the lymph glands accumulated pigment purely in a passive fashion as a filter of the lymph stream coming from organs primarily involved, such as the liver, pancreas, marrow, etc.

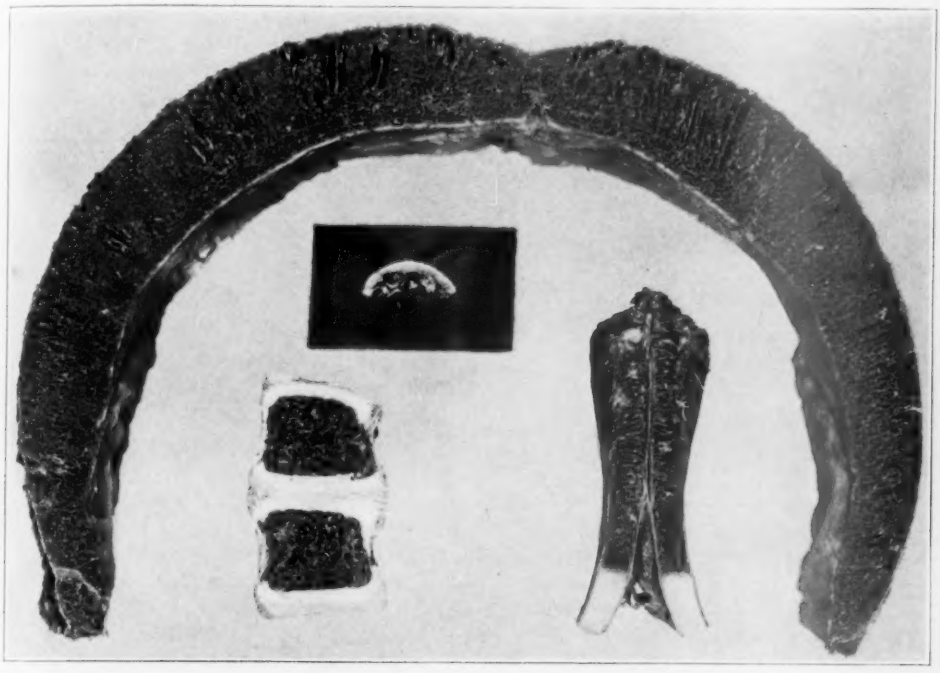


Fig. 6 (case 1).—Coronal section of the calvarium, a rib and costochondral junction, vertebrae and cross-section of the shaft of the femur.

Skeletal System: The calvarium, as already noted, was greatly thickened, measuring from 1.5 to 1.8 cm. in thickness (fig. 6). On section the tables were seen to be widely separated and in large measure obliterated. The outer and inner tables were not distinct. The greater part of the bone was made up of a sponge-like marrow in which there were rather heavy bone trabeculae, having a peculiar arrangement at right angles to the dura. This marrow was of a deep red but seemed to have a chocolate tinting. Through the periosteum the sternum showed this chocolate-brown tint, but on section the red predominated. The sternum was definitely thickened, especially in the manubrium. As previously mentioned, the jaw was thickened, but it could not be examined by section. The ribs presented an extraordinary appearance, showing great thickening, being almost double their normal diameter, and tapering toward the costal cartilages where they appeared to be normal. The line of ossification was normal. On section the ribs presented the

same spongy appearance, as did the calvarium (fig. 6). The greatest thickening in the ribs was found within an inch of the costochondral junction and close to the vertebral column, some of the middle third being more nearly normal. The ribs almost touched each other as they were viewed from within the thorax. The same chocolate tint was made out here as well. The same type of marrow was found in the bones of the vertebrae, but the bones did not seem to be greatly deformed (fig. 6).

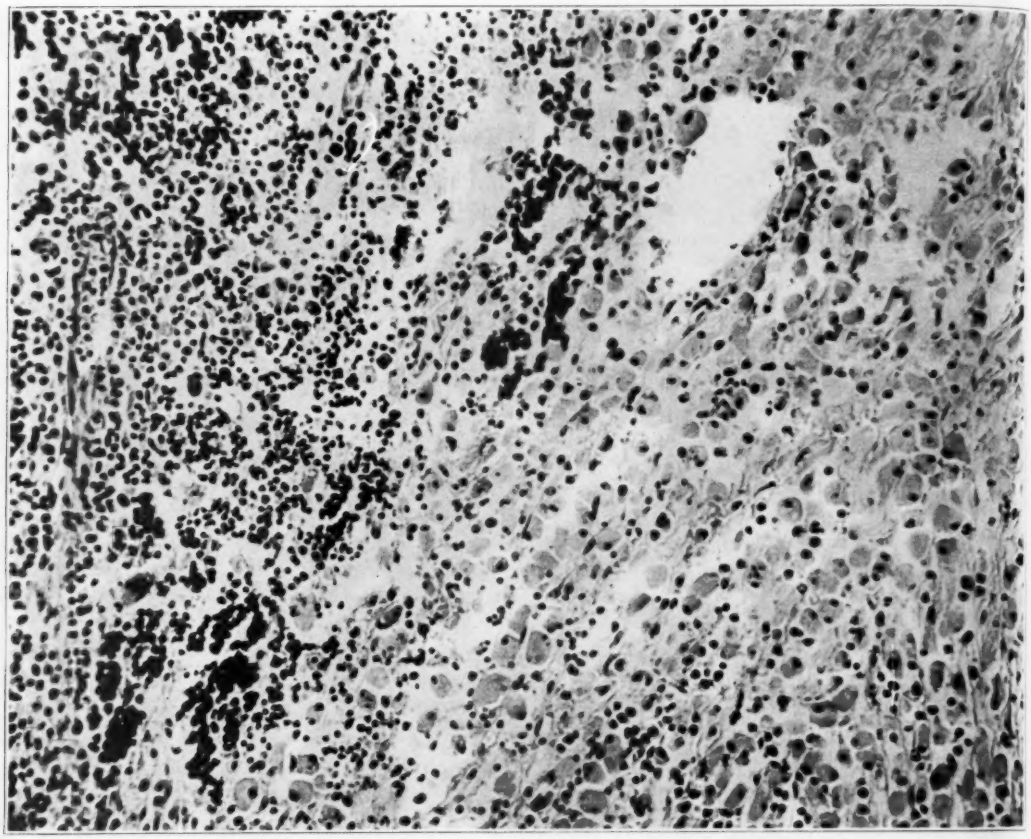


Fig. 7 (case 1).—Photomicrograph of marrow of femur, showing islands of foam cells and hyperplasia of red cells; magnification × 200.

Femur: On section the compact shaft was reduced almost to the thickness of an egg shell, measuring only from 1 to 2 mm. in thickness (fig. 6). All of the enlarged core was made up of hyperplastic bone marrow, containing large spicules but also having a definite chocolate color. The periosteum stripped easily from the shaft.

The general marrow tissue everywhere presented a uniform picture. It was very cellular, and appeared to be tremendously active. Nucleated red cells and related parent cells were obviously numerous. Eosinophils and other myelocytes were numerous, occurring as usual in clusters and islands. Large parent cells of an undefined type were numerous. Megakaryocytes were inconspicuous, probably

somewhat obscured by the tremendous hyperplasia of other elements. They were somewhat small. Here and there in the bone marrow, usually close to nutrient vessels, were nests of foam cells similar to those described in the spleen (fig. 7). They were large cells with relatively small vesicular nuclei and frothy or finely granular cell protoplasm. Occasionally these cells contained blood pigment giving a positive reaction for iron. They did not contain fat-staining substances. It would appear that they were unusual types of phagocytes, although in a measure they may suggest the characteristic cells so numerous in Gaucher's disease.

Large phagocytes very rich in pigment were also a conspicuous feature of this marrow. These phagocytes may have been earlier stages in the development of the foam cells, but they were much more numerous and diffusely scattered throughout all parts of the marrow. Many of them contained small and large grains of pigment and obviously fragments of partly digested red cells. Some of the pigment gave a positive stain for iron, but most of it did not stain for iron. As in the spleen, it was rather striking that this marrow did not contain more pigment giving a positive test for iron. Changes in bony structure were interesting and not easy to explain. In places the trabeculae appeared definitely thinned, but there was no evidence of overactivity of osteoclasts or of an inflammatory reaction such as osteomyelitis. The shafts of the ribs were thinned as in the case of the femur. Outside of the rib shell there was considerable bone marrow tissue growing in the periosteal tissue and splitting the periosteum into many layers (fig. 6). This explains in part the thickening of the ribs and the appearance of bone marrow without the cortical shell of the rib. Probably the reaction with thickening of the calvarium was somewhat similar, and the outer and inner tables of the calvarium were almost obliterated by the cellular spongy marrow. It seems difficult or impossible to explain this type of reaction on the basis of simple hyperplasia and pressure atrophy. The line of ossification between cartilage and bone in the rib gave no evidence of rickets or syphilis. The line was thin and normal, and the histologic elements were of normal appearance.

Suprarenals: The suprarenals were definitely smaller than normal. The cortex was very thin. The medulla was somewhat diminished in amount. These organs were about one fourth of their normal size. They showed no gross evidence of necrosis or degeneration.

In spite of the hypoplasia, the individual elements of the suprarenals appeared to be normal. The outer or glomerular zone of the cortex in some areas showed definite pigment in fine granules, which gave a positive reaction for iron. Other areas were pigment-free or contained a little pigment which did not react for iron. The middle and inner zones of the cortex appeared to be normal. The medulla was well preserved, and showed the usual chromaffin pigment but no pigment that reacted with iron stains.

Thyroid: The thyroid was rather small. Colloid was conspicuous. The gland was quite pale.

The acini appeared rather overactive, and the colloid was somewhat pale, but the lobulation was regular. In many acini the epithelium showed very fine grains of yellow pigment; some of it gave a positive stain for iron and other pigment was negative for iron. The pigment seemed to be more abundant in the inner edge of the epithelium toward the colloid, but no pigment was noted within the colloid.

Parathyroids: There was one parathyroid gland on each side, close to the thyroid gland. They were normal in color and in size.

These glands showed an interesting pigmentation which was very diffuse, involving practically all of the cell protoplasm which contained very fine yellow

granular pigment, almost all of which gave a positive stain for iron. Practically all of the cells in the parathyroid glands were of the basophilic or chief type, and no acidophilic cells were noted.

Hypophysis: The hypophysis was small and very pale; it had a gray, fibrous appearance and did not look cellular.

The pars nervosa showed no unusual pigment and appeared normal. The pars intermedia showed abundant finely granular yellow pigment within the epithelial cells. It stained readily for iron. The colloid, however, was free from pigment. The pars anterior showed scattered acini containing yellow granular pigment which gave a positive test for iron. The pigment, however, was not abundant, and the majority of acini were free from pigment. Within the acini, the pigment was usually observed within the "chief cells" the protoplasm of which took a basic stain.

Thymus: The thymus was diminished in size, as might be expected on account of the general cachexia. It was of uniform texture, pale and not pigmented.

Histologic sections showed evidence of atrophy. Hassall's corpuscles showed no pigmentation. Within the reticulum were seen occasional yellow grains of pigment, much of which stained sharply for iron.

Brain: The brain weighed 1,050 Gm. It appeared to be normal in all respects.

The meninges and brain tissue were seen to be normal on section after complete fixation. The sections taken from the various parts of the cerebral hemispheres appeared normal. The pons, medulla and cerebellum were likewise normal. There was no evidence of any unusual pigmentation in any part of the brain stem.

Sections from the brain, pons, medulla and the region of the pineal gland showed normal tissue, with no unusual pigment. Sympathetic ganglions observed in other sections showed no unusual pigmentation.

Case 2.—*History.*—In P. G., aged 2 years and 3 months, a brother of the patient in case 1, the onset of the illness occurred during the latter part of the first year of life, when the patient was noted to be unusually pale and anemic and to possess an enlarged spleen. He was feverish and fretful at times, and seemed to be growing weak. In June, 1930, the abdomen became enlarged and dental caries appeared, and in November, 1930, an infection of the mouth occurred. From June, 1930, until January, 1931, the patient was under observation at the Clifton Springs Sanitarium, where repeated examinations of the blood were made. Here the diagnosis of anemia of the von Jaksch type was made.

The birth was normal, and the weight at birth was 9½ pounds (4,309 Gm.). For seventeen months the infant was breast fed. Since 6 months of age, orange juice had been given irregularly. The administration of cod liver oil was started when the patient was 18 months; cereals, at 6 months, and vegetables and eggs, at 1 year. Since January, 1930, the diet had consisted of a good anti-anemia regimen, including liver, fruits, eggs, vegetables, etc. The patient took this diet well.

Physical and mental development were normal. Dentition began at 7 months. The patient walked and talked at 1 year of age. Infections occurred in the form of frequent colds in the head. In January, 1931, the patient was hospitalized because of bronchopneumonia. He had escaped the usual communicable diseases.

The father, aged 34, and the mother, aged 25, were normal Italians. A sister 7 years old was well, but another sister (case 1) had recently died at the age of 5 years from a similar disease.

Physical Examination.—On admission to the hospital the patient presented the clinical appearance described as typical of so-called erythroblastic anemia (Cooley). He was 2¼ years old, an Italian, chronically ill, fretful and resistant to examina-

tion. The features were distinctly mongoloid (fig. 8). There was orbital edema; the face was pale and oriental in appearance. The temperature was 37.4 C. (99.3 F.), the pulse rate, 124, and the respiratory rate, 40. The skin was of an ashen pallor, moist and smooth. There was no eruption and no jaundice. The anterior cervical and inguinal lymph nodes were palpable but not definitely enlarged. The skeletal bones were normal, except for the beading of the costochondral junctions. The head was square and large. The bosses were prominent, and a fine coat of hair extended well onto the forehead.

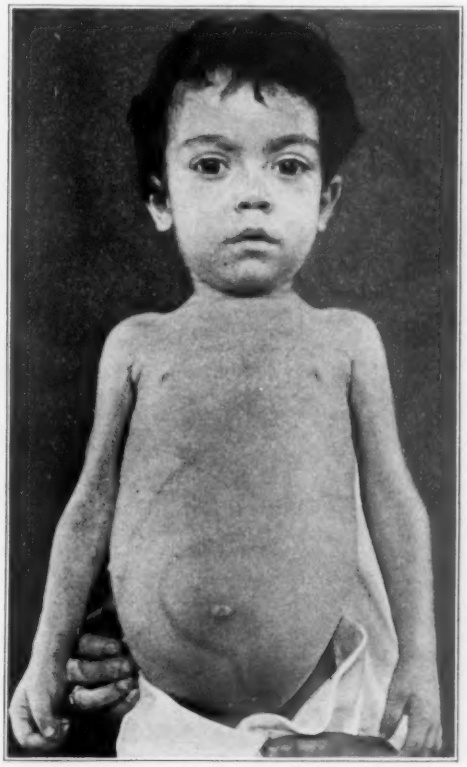


Fig. 8 (case 2).—The patient had a large liver and spleen and mongoloid features.

The eyes, ears and nose were normal. The lips were pale, the tongue coated. The tonsils were large and pale, and the teeth were carious. The neck was normal.

The chest was symmetrical. The breath sounds were normal. The heart was enlarged to the left. The sounds were of good quality. There was a soft systolic murmur at the apex, not transmitted. The pulses were regular and equal; the rate, 150. The blood pressure was 90 systolic and 60 diastolic.

The abdomen was noticeably protuberant and tense. The spleen was of an enormous size, filling the entire left side of the abdomen; it was hard, smooth and only slightly tender (fig. 8). The liver extended three fingerbreadths beneath the costal margin. The genitals were normal, as were also the deep tendon reflexes.

Roentgen Examination.—Roentgen examination was made by Dr. W. W. Fray on Feb. 3, 1931. He reported: "The calvarium appears thickened, especially over the frontal area. Here the tables are thinned to a sharply contoured line. The thickening of the calvarium in this region appears to be due to the diploe. There is a faint suggestion of radial striation. The findings in the various bones suggest those seen in long standing anemia in which the marrow has become hyperplastic."

Concerning the extremities he reported that they "show three characteristics which commonly affect all the bones examined; a thinning of the cortex, enlarge-

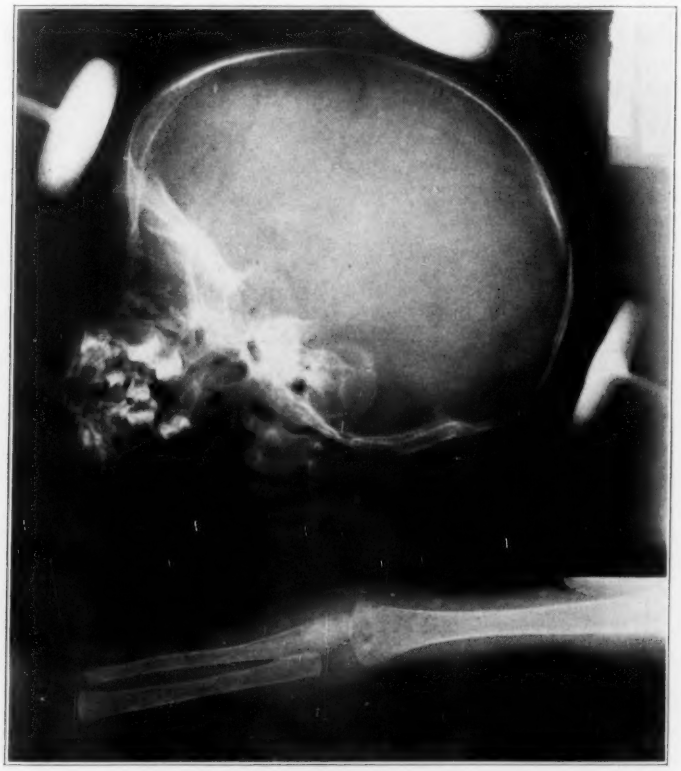


Fig. 9 (case 2).—Roentgenogram showing bone changes which are slight in the skull. The bones of the arm show atrophy of the trabeculae.

ment of the medullary cavity and an increase in the diameter of the shafts of the bones. All the bones show coarse, irregular trabeculation. In general, the calcium content is diminished."

Laboratory Data.—Examination of the blood made on February 3, showed: hemoglobin, 40 per cent; red cells, 3,220,000, and white cells, 45,700; of these 23,900 were found to be nucleated red cells, the actual number of white cells being 21,800. The differential count made with the supravital technic (200 cells) showed: polymorphonuclears, 43.0 per cent; lymphocytes, 30.0 per cent; mononuclears, 18.5 per cent; basophils, 0.5 per cent; eosinophils, 2.5 per cent, and myelocytes, 5.5 per cent.

A smear made with Wright's stain showed a textbook picture of all the variations in red blood cells from megaloblasts to degenerated cells. There were 110 nucleated red cells for every 100 white cells counted. There were marked variations in the size and shape of the cells, moderate achromia, considerable polychromatophilia, etc. The number of platelets seemed to be considerably reduced.

A fragility test was made on February 11, with hypotonic salt solution. Hemolysis began at 0.34 per cent and was complete at 0.20 per cent.

March 30, the resistance of the red cells to sodium oleate in a dilution of 1:1,600 showed complete hemolysis of the patient's and of the control's cells; in a dilution of 1:3,200, no hemolysis of the patient's and complete hemolysis of the

TABLE 2.—*Observations on the Blood in Case 2**

Date	Hemoglobin, per Cent	Red Blood Cells	White Blood Cells	Polymorphonuclears, per Cent	Myelocytes, per Cent	Lymphocytes, per Cent	Monocytes and Transitionals, per Cent	Number of Nucleated Red Cells per Hundred White Cells
2/ 2/31	40	3,220,000	82,000	27.0	...	53.0	20.0	Many
2/ 3/31†	40	.....	45,700	45.5	5.5	30.0	18.5	110
2/ 6/31	50	4,240,000	40,000					
2/ 7/31	55	4,450,000	30,000					
2/ 9/31	50	3,700,000						
2/16/31	45	2,250,000	19,300	64.0	...	27.0	9.0	
2/18/31†	48	3,410,000	30,050	74.0	4.0	18.0	3.0	10
2/18/31	..	.....	23,100	68.0	1.5	18.0	12.5	6
2/20/31	49	3,550,000	15,550					
2/23/31	43	3,730,000	26,000	67.0	...	26 0	7.0	
2/28/31	38	2,600,000	24,200	57.0	...	24.0	19.0	Few
3/11/31†	22	1,500,000	22,300	40.5	7.5	46.5	5.5	3
3/13/31†	35	2,410,000	17,080	41.5	3.5	46.0	7.0	
3/16/31	26	1,550.000	11,200	33.0	3.0	59.0	4.0	
3/16/31†	..	.....	.....	29.5	2.0	64.5	4.0	
3/20/31†	30	1,650,000	8,300	31.0	2.5	58.0	7.5	6
3/23/31	21	980,000	7,200					
3/25/31†	27	1,720,000	5,400	12.0	5.0	72.5	10.5	5
3/29/31†	20	1,070,000	5,200	9.0	6.0	73.0	12.0	4
4/ 1/31	23	1,570,000	3,050					
4/ 5/31†	30	2,400,000	7,050	15.5	12.0	56.0	15.5	70
4/ 8/31†	25	1,760,000	6,840	8.0	9.0	71.0	11.5	
4/12/31†	18	1,230,000	3,500	7.0	9.0	63.0	21.0	

* The terminal fall of the hemoglobin and red blood cells is again apparent. A tendency toward terminal agranulocytosis is noted. Many nucleated red blood cells appeared in the peripheral blood. Smears revealed a textbook picture of all the variations in red blood cells from megaloblasts to degenerated cells. Marked variation in the size and shape of the erythrocytes, moderate achromia and considerable polychromatophilia were features. At times platelets were abundant; at times, scarce. The observations made by the supravital technic are thought to be especially accurate.

† Differential counts were made by supravital technic.

control's cells occurred. On February 4, the clotting time was two and a half minutes retractible normal and the bleeding time, five and a half minutes; the van den Bergh test showed 1.8 units of bilirubin (on March 30, 1 unit); the icterus index was 12 units on February 4 (on March 30, 8 units).

On February 2, the fibrinogen was 0.187 per cent; the pigments, 0.047 mg. per hundred cubic centimeters (on March 30, 0.036 mg.); the serum protein, 7.95 per cent; the red cell volume, 25 per cent; the calcium, 9.2 mg., and the phosphorus, 4.3 mg. per hundred cubic centimeters of blood. The Wassermann and Kahn tests both gave negative results. Urinalysis showed: acid, 1.015, and no albumin or sugar, and the guaiac test negative.

Microscopic examination gave normal results. On one occasion no urobilin was noted; at another time, a faint trace.

Cultures from the nose and throat were negative for B. diphtheriae. No hemolytic streptococci were found. Skin tests with tuberculin (human) were negative. The Schick and the Dick tests gave negative results.

Examination of the stool made on February 3 showed that it was well formed and brown; there were no parasites or ova. Microscopic examination gave normal results.

On February 4, the basal metabolic rate was normal.

On March 26, gastric analysis made during fasting showed no free hydrochloric acid and a combined acidity of 70; an analysis made thirty minutes after the ingestion of 25 cc. of a 7 per cent solution of alcohol showed no free hydrochloric acid and a combined acidity of 60.

Course.—During the period of observation from Feb. 2, 1930, until April 15, 1931, no definite evidence of improvement was noted. Thirteen transfusions of

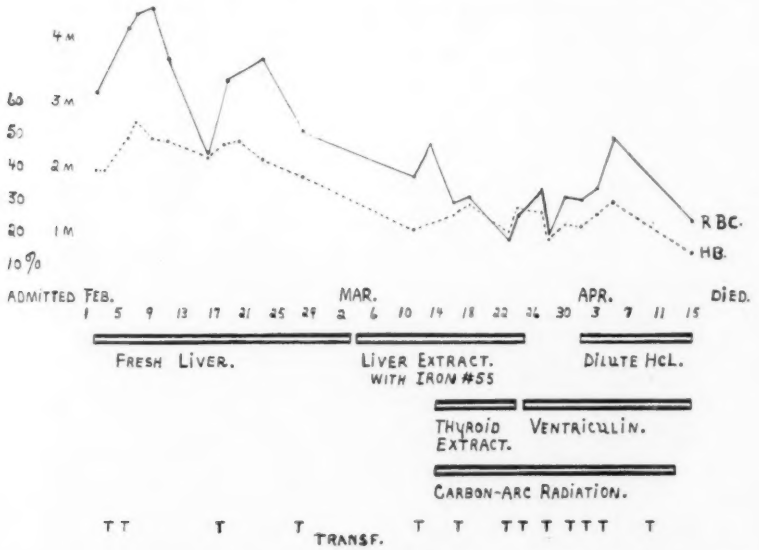


Fig. 10 (case 2).—Red cells and hemoglobin curves and therapy. The following treatment was given: 50 Gm. of fresh liver daily; liver extract equivalent to 125 Gm. of liver daily; 0.015 Gm. of thyroid extract three times a day; five drops of dilute hydrochloric acid three times a day, and 1 vial of ventriculin daily. Eleven treatments with carbon arc radiation were given from one to ten minutes, with the front and back being exposed at a distance of 6 feet (15.2 cm.).

blood had no effect on the anemia. The pallor continued, and the patient gradually weakened. Several attacks of infections of the upper respiratory tract occurred, and at one time bronchitis developed. At no time did hemorrhage occur.

It is significant that all therapy directed against the anemia failed. The patient received 50 Gm. of liver daily for twenty-eight days after admission to the hospital and for several months previously he had received varying amounts of it daily. The administration of liver extract with iron and ventriculin also had no effect.

Because of the fact that in case 1 the endocrine glands were so abnormally pigmented, it seemed of interest to try some of the extracts in this case. Only thyroid extract was tried, however, without effect. Because of the absence of free

hydrochloric acid in the patient's stomach, dilute hydrochloric acid was given by mouth during the latter days of life. No beneficial effect was noticed. Over a period of a month, twelve treatments with carbon arc radiation were given.

Splenectomy was not performed because of the patient's poor general condition and the enormous size of the spleen and because of the questionable benefit observed in another patient with this condition who was under our care at that time.

Nothing of unusual interest occurred in the blood picture. Except for a tendency toward agranulocytosis in the latter days, the blood picture throughout the course, the features of the patient, his nationality, the evidence obtained from the roentgenographic studies of the skull and long bones and the enlarged spleen seemed to establish beyond reasonable doubt the clinical diagnosis of von Jaksch's anemia, recently termed by Cooley erythroblastic anemia.

The patient was removed from the hospital on April 15, and died two days later. Permission for autopsy was denied.

Clinical Summary of Cases 1 and 2.—The clinical features in cases 1 and 2 were almost identical. In brief, the significant features were: a sister and a brother of Italian parentage exhibiting progressive anemia, originating in the latter part of the first year of life; splenomegaly; showers of nucleated erythrocytes in the peripheral blood; peculiar mongoloid facies; changes in the skull, ribs and long bones, and failure to respond to continuous and varied anti-anemic diets and therapy. They died at the ages of 5 and 2½ years, respectively. Nothing in the history indicated that anemia existed at birth, and there is evidence that rickets, syphilis and chronic malaria were not etiologic factors. It is improbable that any of the known vitamins were deficient in the diet.

CASE 3.—Since from birth until the time of writing, the patient, J. S., has been continuously under our observation either in the hospital or in the out-patient department, the history, physical findings and course can probably best be presented by noting the significant events in chronological order.

History.—Oct. 29, 1928: J. S., a boy, was delivered by spontaneous labor; he weighed 2,620 Gm. The prenatal period was normal. The parents were healthy Italians. The father was said to have had malaria in 1922, from which he had made a good recovery. The mother's diet throughout pregnancy had not been deficient. There was no evidence of clinical or of serologic syphilis in any of the three. No other pregnancies had occurred.

The infant nursed well and apparently was normal physically. The liver and spleen were not palpable, and there was no pallor. At the age of 2 weeks, the measurements were as follows: circumferences of the head, 36 cm.; that of the chest, 32 cm.; the length, 50 cm.

Nov. 12, 1928 to July 8, 1929: Eleven visits to the out-patient department were made. The patient was breast fed entirely until the third month, when the feeding of cereal was started; cod liver oil and 8 cc. of orange juice had been given daily since 2 weeks of age.

Nov. 22, 1928: A small umbilical hernia was noted.

Feb. 28, 1929: A small left hydrocele was present.

April 5: Supplementary feedings of cow's milk were started.

May 31: At the age of 7 months, the first illness, an acute infection of the upper respiratory tract, diarrhea, otitis media, pallor and listlessness occurred, and there was failure to feed normally.

June 26: The sclera seemed tinted; the skin was sallow and pallor was noted. Examination of the blood revealed hemoglobin, 40 per cent, and 3,670,000 red cells. The liver and spleen were palpable. There was a systolic murmur.

First Admission (July 9 to August 8).—The patient was 8 months of age. Jaundice, pharyngitis, pallor, systolic murmur, enlargement of the spleen and liver and hydrocele of the left side were noted.

Laboratory Data.—Examination of the blood showed: hemoglobin, 45 per cent; red cells, 3,800,000, and white cells, 14,500. A smear showed marked anisocytosis, poikilocytosis and achromia, and 10 nucleated red cells per hundred white cells. The differential count showed: lymphocytes, 55; monocytes, 14; polymorphonuclears, 28; polymorphonuclear eosinophils, 1, and polymorphonuclear basophils, 1. No parasites were noted. Platelets were abundant. Results of further studies of the blood cells are shown in table 3.

The Wassermann and Kahn tests gave negative results. Both parents were also normal. The blood group of both parents and of the patient was type II (Moss).

A test for hemolysis showed that the resistance of the red cells to hypotonic salt solutions was normal. The bleeding time was three and a half minutes; the clotting time, three and a half minutes. The icterus index was 6 mg. of bilirubin per hundred cubic centimeters. The van den Bergh test showed 2.2 units.

The Schick and Dick tests and the intradermal test with 0.1 mg. of tuberculin (human and bovine) gave negative results.

The urine was normal.

July 9: The calcium was 9.45 mg. and the phosphorus, 3.67 mg. per hundred cubic centimeters.

August 5: The calcium was 11.3 mg. and the phosphorus, 4.2 mg. per hundred cubic centimeters.

July 15: Roentgen examination of the skull gave normal results.

During this admission, the patient received three intraperitoneal transfusions of blood. The spleen and liver decreased rapidly in size. The general condition improved markedly. The patient was discharged on August 8.

August 9 to September 12: The patient was followed in the out-patient department; there were five visits to this department.

A diet of milk, cereal, vegetables, orange and tomato juice, liver and cod liver oil was given, also yeast. The patient did well for a while, and then he became weaker. He was unable to sit without support. The spleen was again enlarged.

Second Admission (September 12 to November 22).—Physical examination revealed a poorly developed Italian boy, with red hair; the glands were generally enlarged. The anterior fontanel was closed. The liver and spleen were greatly enlarged. Pallor was noted. The impression was that splenic anemia of von Jaksch's type was present. The van den Bergh test showed 2.2 units. There was 4.4 mg. of phosphorus per hundred cubic centimeters of blood.

September 16: Roentgenograms of the chest revealed a slightly dilated heart.

September 17: A fragility test of the red blood cells with hypotonic salt solution showed that hemolysis began at 0.46 per cent and was complete at 0.28 per cent. No tendency of these cells to sickle was noted, even when they were subjected to carbon dioxide.

September 23: Roentgen examination of the skull gave normal results. The wrist was coarse, with trabeculation of the bone.

October 15: Examination of the blood showed: calcium, 10 mg. per hundred cubic centimeters and serum proteins, 7.85 mg.

October 29: On roentgen examination of the skull, changes of thickness were noted for the first time. The patient was 1 year of age.

During this admission, it became reasonably certain that the condition was erythroblastic anemia (Cooley). After four intravenous transfusions and other treatments, the patient seemed to improve. The spleen failed to regress, however. The child suffered from otitis media, pharyngitis, bronchitis and diarrhea. Cultures of the stools gave negative results.

November 22 to Jan. 24, 1930: Observations made at eight visits to the outpatient department revealed the fact that the patient did well for a few weeks; the appetite was good, and the spleen became smaller.

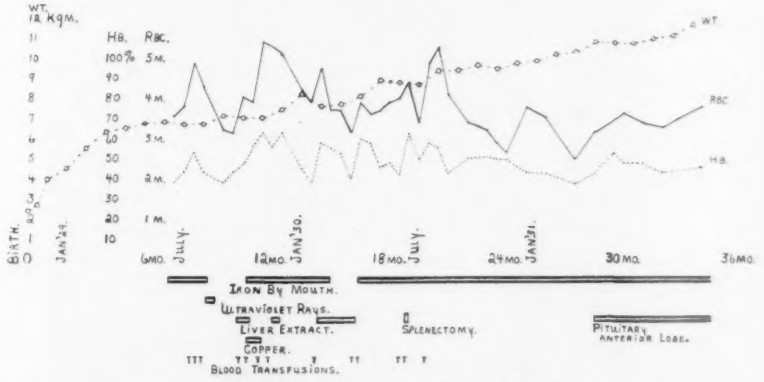


Fig. 11 (case 3).—Red cells, hemoglobin and weight curves. Throughout life, the diet contained an ample supply of the various vitamins. Since the patient was 6 months of age, he has been fed whole liver and vegetables regularly. The following therapy was administered: 0.2 Gm. of saccharated ferrous carbonate three times daily; six treatments with ultraviolet rays; liver extract (Lilly no. 55, represents 50 Gm. of liver); 0.02 Gm. of copper daily; 0.13 Gm. of pituitary gland (anterior lobe) three times daily, and thirteen transfusions of blood, a total of 1,700 cc.

Dec. 29, 1929: A cold in the head, fever and pharyngitis developed. The patient became weaker and pale.

Third Admission (Jan. 24 to March 26, 1930).—March 7: Examination of the blood showed: calcium, 9.9 mg., and phosphorus, 4.6 mg. per hundred cubic centimeters.

March 11: Acute bronchitis developed.

March 17: The van den Bergh test gave 2.2 units of bilirubin. The icterus index was 7. Blood cholesterol was 0.087 per cent (about one-half normal) and the total fatty acids, 0.411 per cent (high normal).

March 18: Roentgenograms showed marked thickening of the skull over the frontal region, affecting chiefly the outer table.

March 26: The condition of the patient on discharge from the hospital was favorable. Three transfusions of blood were given during this period.

Analysis of the blood showed no phospholipids, 144 mg. of cholesterol and 413 mg. of total fatty acids per hundred cubic centimeters of plasma and 437 mg. of phospholipids, 160 mg. of cholesterol and 442 mg. of total fatty acids per hundred cubic centimeters of red cells.

Dr. W. R. Bloor reported that the amount of cholesterol in the plasma was normal for a child (normal ranging from 100 to 200 mg.), and that the amount of cholesterol in the cells was low, though not greatly reduced (normal being from 170 to 230 mg.). The phospholipids in the corpuscles were normal. The amount of total fatty acids was a high normal in both the plasma and the corpuscles.

March 27 to May 31: The patient was seen on six different occasions in the out-patient department. He was doing well on a varied diet, including vegetables and liver.

Fig. 12 (case 3).—Patient in case 3, showing mongoloid features.

April 16: The patient had a slight cold in the head.

April 30: The spleen and the liver were not palpable.

May 9: Cough, coryza, vomiting and otitis media developed.

May 31: Enlarged cervical glands were noted. The spleen was palpated three fingerbreadths below the costal margin. The liver was palpable.

Fourth Admission (May 31 to July 12).—June 1: Chemical analysis of the blood showed: total lipids, 527 mg.; cholesterol, 99 mg.; total fatty acids, 428 mg. and phospholipids, 137 mg. per hundred cubic centimeters.

June 10: Splenectomy was performed. A specimen of tissue was removed from the liver for a biopsy. The postoperative course was uneventful.

June 13: Examination of the blood plasma showed: total lipids, 600 mg.; cholesterol, 108 mg., and total fatty acids, 492 mg. per hundred cubic centimeters.

June 24: A roentgenogram taken of the skull in a lateral position showed further thickening of the calvarium, 1.4 cm.; three months previously, it had measured 1.0 cm. Roentgen examination of the humerus showed abnormal growth and development of the bone and well delayed epiphyseal development.

July 2: The circumference of the head was 48 cm.; that of the chest, 51.5 cm., and that of the abdomen, 49 cm.; the length was 78 cm.

July 10: The icterus index was 5 units. An analysis of the spleen made by Dr. W. R. Bloor showed: dry substance, 21 per cent; phospholipids, 1.44 per cent; cholesterol, 0.30 per cent; fat, 0.84 per cent, and $\frac{\text{Phospholipid}}{\text{Cholesterol}} = 4.8$. Exam-

Fig. 13 (case 3).—Roentgenogram of skull, showing radial markings; the arm showed atrophy of the trabeculae and shaft.

ination of the blood serum proteins (measured by refractometer) showed 8.05 per cent; albumin, 5.55 per cent; pseudoglobulin, 2.24 per cent; euglobulin, 0.78 per cent; total proteins, 8.57 per cent. The patient received three transfusions of blood during this hospitalization. Following splenectomy, the characteristic shower of nucleated red blood cells appeared in the peripheral blood.

July 13 to July 18: The patient made twenty-one visits to the outpatient department. He did well and gained weight slowly.

December 19: The patient was beginning to walk, and said a few words; he was 25 months old. Occasional attacks of coryza occurred.

March 31, 1931: He fell and injured the right leg so that he was unable to stand on it. Roentgenograms revealed a slight periosteal injury to the upper part of the fibula and the lower part of the tibia of the right leg. Osteoporosis was noted; a cast was applied and removed on April 28.

June 30: The patient was doing well. He was playful and took food well.

Fifth Admission (July 18 to July 25).—The patient was brought to the hospital for a check-up examination.

July 20: Roentgenograms showed characteristic radial striations between the tables of the skull. Roentgenograms taken of the humeri showed coarse trabeculation; the width of the upper part of the shaft was increased, and the cortex of the bone remained thin and shell-like (fig. 13).

Examination of the blood showed: icterus index, 40 units; van den Bergh test, 2.3 units; plant pigments, 0.058 mg.; cholesterol, 180 mg.; lecithin, 110 mg., and total lipids, 563 mg. per hundred cubic centimeters.

July 24 to October 10: During this time, the patient was seen in the clinic of the out-patient department on three occasions. He had received no transfusions of blood since July 10, 1930. The hemoglobin remained around 50 per cent, and

TABLE 3.—*Gastric Analysis Made in Case 3 on July 21, 1931*

	Free Hydrochloric Acid	Total Acidity, per Cent	Lactic Acid
Fasting	0	7.5	++
After 7 per cent alcohol			
Meal 45 minutes	0	1.5	
75 minutes	0	15.0	++
105 minutes	0	15.0	+
135 minutes	0	10.0	+

the number of red cells was between 3,500 and 4,000 per cubic millimeter. Though he had been able to maintain this level without the aid of transfusions, it was uncertain that he would continue to do so.

Comment.—The evidence submitted justified the clinical diagnosis of erythroblastic anemia (Cooley). The case was interesting because it was possible to study it in detail from the date of birth. It seems improbable that dietary deficiency, rickets or syphilis produced the condition present. It is regrettable that blood counts were not obtained during the first few weeks of life. The initial weight curve and clinical course suggest that the first evidence of the disease occurred about the sixth month of life.

Anatomic Data.—Spleen: The spleen, removed at operation, presented the usual gross appearance. The malpighian bodies were small; the size or weight were not recorded.

There was a moderate increase in connective tissue throughout the splenic pulp. The malpighian bodies were inconspicuous and smaller than normal, but showed no abnormalities. Eosinophils were moderately numerous. Some of them may have been myelocytes, and in this case the spleen may have participated slightly in the marrow reaction, but there were no conspicuous nests of nucleated red cells, megakaryocytes and other indications of true marrow activity. It is possible to explain it all on the basis of filtration of cells from the circulation. A few foam cells previously described were found in the pulp. They were large mononuclear cells with small vesicular nuclei and a frothy or foamy granular protoplasm. Some

of these cells contained pigment that gave a positive reaction for iron. On the whole, this section showed a good deal of pigment, yellow and granular, that gave a positive stain for iron. It was found in large phagocytes and pulp cells. Some iron-containing pigment was noted in the endothelium lining the sinusoids. As compared with the spleen in case 1, it was obvious that this was a much earlier stage in the development of the terminal picture, there being less diffuse fibrosis and a much more cellular pulp. The character of pigment and its distribution was somewhat different.

TABLE 4.—*Observations on the Blood in Case 3**

Date	Hemoglobin, per Cent	Red Blood Cells	White Blood Cells	Polymorphonuclears, per Cent	Myelocytes, per Cent	Lymphocytes, per Cent	Monocytes and Transitionals, per Cent	Number of Nucleated Red Cells per Hundred White Cells
6/26/29	40	3,670,000						
7/ 9/29	45	3,800,000	14,600	30	..	55	14	10
8/ 5/29	45	4,400,000	8,600	29	..	64	7	
9/12/29	40	3,300,000	16,720	23	..	70	7	12
10/ 1/29	49	4,140,000	14,500	43	..	52	5	43
11/ 2/29	65	3,470,000	16,200	25	..	72	2	
12/29/29	47	4,310,000	29,800	20	2	68	3	
1/25/30	65	5,090,000	10,100	27	2	65	4	
2/14/30	57	3,880,000	12,300	36	..	54	4	
3/14/30	42	3,250,000	15,000	45	12	33	10	1
4/16/30	60	3,700,000	11,000	37	..	55	8	
5/31/30	38	3,840,000	13,950	33	..	58	9	5
6/11/30	Splenectomy							
6/11/30	66	5,070,000	12,900	63	..	16	20	35
6/22/30	60	4,620,000	18,000	49	..	35	16	40
6/27/30	50	3,650,000	88,000	54	..	25	21	196
7/12/30	60	5,070,000	63,800	37	..	36	27	140
9/26/30	52	3,500,000	65,000	32	5	37	25	152
12/12/30	45	3,950,000	105,600	33	..	60	7	210
3/ 3/31	40	2,630,000	116,000	43	..	46	9	145
4/28/31	55	2,690,000	37,000	35	..	52	14	52
6/20/31	50	3,500,000	40,800	26	..	62	12	
7/18/31	45	3,450,000	27,600	36	..	59	5	
7/24/31	..	.....	.....	52	1	42	5	
9/11/31	48	3,930,000						
10/ 6/31	30	2,600,000	33,600	38	..	59	3	200

* These blood counts are representative of more than one hundred differential counts made during the period of observation. They are modified no doubt at times by the use of transfusions of blood (fig. 11). In general, they closely resemble the counts in cases 1 and 2 (tables 1 and 2). An interesting demonstration is the characteristic "showering" of nucleated red blood cells after splenectomy (June 10).

Liver: At the time of splenectomy a section of liver was excised for study. The liver cells in general were normal. There was no increase in connective tissue. There were more nucleated cells than normal cells within the liver capillaries; some of them were nucleated red cells. The liver epithelium in the marginal half of the lobule about the portal spaces showed abundant finely granular yellow pigment within the epithelium. This pigment stained sharply for iron. A little of this pigment was found in the central portion of the liver lobule within the hepatic epithelium. The Kupffer cells contained rather coarse granular refractile pigment which did not give a positive stain for iron. In all respects this pigment corresponded closely to that noted in case 1 and was conspicuously different from the pigment observed in Kupffer cells in other types of anemia.

COMMENT

The marrow changes are extreme and involve all of the cellular elements. The parent marrow cells are very numerous and red cell forming elements, very hyperplastic. Eosinophil myelocytes and related chain cells are conspicuous. The megakarocytes are inconspicuous and rather small but evidently functioning properly as the platelets are not abnormal. Phagocytes are numerous and large and give evidence of incomplete marrow function and active cell break-down. In this respect, especially the marrow of this disease is like the marrow in pernicious anemia. The large phagocytes with foamy protoplasm (fig. 7) are like those described in Gaucher's disease. These cells give no evidence of fat or cholesterol droplets and may contain some iron-reacting pigment. The amount of cholesterol of the blood in case 1 was not high. Identical foam cells have been noted in the spleen in similar cases and have been reported by Whipple, Reeves and Cobb.[5]

From an analysis of anatomic evidence, Whipple,[6] in 1922, suggested that pernicious anemia should be studied as a disease due to a lack of something essential to the construction of red cells rather than a disease due to toxic destruction of blood. The marrow in this disease, illustrated in figure 7, resembles that of pernicious anemia in some respects and suggests the possible lack of something essential for normal development of marrow. This hypothetical substance is not present in liver, as a liver diet has no influence on the blood or marrow picture in this disease. However, this does not eliminate the possibility that some other food substance may contain the missing element.

The unusual pigmentation described in case 1 is much like the pigmentation of hemochromatosis about which it may be appropriate to note the following: Hemochromatosis with the familiar visceral pigmentation was thought to be a disease associated with much destruction of blood which was held responsible for the pigment deposit in the body tissues. Sprunt [7] was the first to point out that there was no evidence of any destruction of blood and increase of pigment from this source. He suggested that the disease was associated with a fundamental disturbance of pigment metabolism. One of us (Dr. Whipple) was associated with Dr. Sprunt during his study of hemochromatosis, and was therefore much impressed with the distribution of pigments in case 1.

---

5. Whipple, A. O.; Reeves, R. J., and Cobb, C. C.: Ann. Surg. **88**:380, 1928.

6. Whipple, G. H.: Pigment Metabolism and Regeneration of Hemoglobin in the Body, Arch. Int. Med. **29**:711 (June) 1922.

7. Sprunt, T. P.: Hemochromatosis: A Report of Three Cases and a Discussion of the Pathogenesis, Arch. Int. Med. **8**:75 (July) 1911.

Pigment distribution in case 1 is not exactly similar to that recorded for hemochromatosis. In case 1, no pigment of any kind was found in the smooth muscle of blood vessels or heart muscle. There was no pigment in the mucosa of the small or large intestine. The pigment deposit was much less in amount and the accompanying fibrosis very slight as compared with hemochromatosis.

We noted conspicuous similarities in pigment deposit in case 1 and in the usual case of hemochromatosis. Iron-staining pigment is present in the salivary glands, mucous glands of the mouth and bronchi, Bruner's glands and various ductless glands in both conditions.

We recorded also in case 1 the presence of a yellow granular pigment rather refractile, giving a negative stain for iron, found in various parts of the lymph glands, where some of it gave a reaction for hemofuscin. This was obviously a different pigment, probably older and more closely related chemically to bilirubin. This yellow granular pigment not giving an iron stain was present also in the Kupffer cells of the liver, in the endothelium of the sinusoids of the spleen and many other places, as already noted.

Pigment in the liver and spleen is noted in various reports of this disease in the literature, but these records give no evidence that a special study of pigment was carried out. Cooley, Witwer and Lee [8] reported the presence of pigment in the liver and spleen, but did not state whether or not it gave a stain for iron. Stillman [9] described the histology of the spleen but did not mention pigment. Wollstein and Kreidel [3] gave a report of the splenic pathologic process noted in several cases and at one autopsy, in which pigment was noted in the liver and spleen, some of which reacted with an iron stain.

It may be interesting to review the pigment abnormalities in a case of childhood aplastic anemia. The liver cells contained fine grains of pigment which gave a positive test for iron, but the Kupffer cells showed large amounts of pigment which also gave a strong stain for iron. Iron-staining pigment was abundant in the spleen, and we observed no pigment which did not react with iron stain. The pancreas and kidneys, the gastro-intestinal tract and all ductless glands were quite free from any sort of pigment. This obviously was a totally different picture of distribution of pigment. Pigmentation in aplastic anemia was mentioned in a paper by Smith.[10]

---

8. Cooley, T. B.; Witwer, E. R., and Lee, Pearl: Anemia in Children with Splenomegaly and Peculiar Changes in the Bones, Am. J. Dis. Child. **34**:347 (Sept.) 1927.

9. Stillman, R. G.: Am. J. M. Sc. **153**:218, 1917.

10. Smith, L. W.: Report on an Unusual Case of Aplastic Anemia, Am. J. Dis. Child. **17**:174 (March) 1919.

The spleen in this disease received considerable attention, possibly more than is justified by its importance. We believe that the organ reacts largely in a passive manner, and that the changes are different when the organ is examined early in the disease than when it is examined late. Early in the disease the fibrosis of the pulp may be inconspicuous, and marrow cells are abundant; there is also a good deal of pigment giving a stain for iron. Late in the disease, the organ is very fibrous, with small malpighian bodies and diffuse increase of connective tissue throughout the pulp. The sinusoids are dilated and thickened, with conspicuous endothelial lining cells which may contain peculiar pigment (case 1). Cells of all sorts are inconspicuous in the pulp, and there is little or no evidence of activity. The organ looks as though it had been damaged by some unknown factor (fig. 1). Splenectomy does not appear to modify the clinical picture, but it does cause an interesting increase in the nucleated red cells of the peripheral blood.

The terminology for this disease is unsatisfactory, particularly if the term von Jaksch anemia is used, in which group a variety of diseases have been reported in the literature. Cooley had described a clinical entity, and it may be wise to use his name to distinguish this disease. We do not like the term "erythroblastic anemia" used by Cooley, as there is nothing especially characteristic about this feature of the blood. The disease is limited almost wholly to Italians, Greeks and Syrians, i. e., to the people originating about the Mediterranean Sea. For this reason the term "thalassemia," derived from the Greek θάλασσα, meaning the great sea and used to designate the Mediterranean, may have an appeal. Mediterranean disease or anemia likewise might be appropriate. As the anemia is only one of several factors in this disease, the term Mediterranean disease might be most accurate and comprehensive.

Because of our special interest in pigment abnormalities in this disease and other conditions, we would be very glad to study autopsy material sent to this school and to report in detail our observations to the department or physician concerned.

SUMMARY

The three cases reported clinically evidently belong in the disease group described by Cooley as "erythroblastic anemia."

The bone marrow changes are typical and suggest a process analogous to pernicious anemia. It may depend on a lack of some unknown material.

The changes in the bone we cannot believe are simply an adaptative reaction to marrow hyperplasia, but we suggest that these abnormalities

may be due in part to some fundamental metabolic disturbance of the order of the abnormalities of the bone in scurvy or acromegaly.

Pigment abnormalities may be extreme (case 1) or slight (case 3), but if shown to be a constant factor in this disease, they suggest some fundamental change in the method of handling body pigment.

One may think of all these abnormalities as related and due to some racial or inherited defect. Once this defect is understood, remedial adjustment may be a possibility, and a study of every factor of internal metabolism is desirable.

As the terminology of this disease is unsatisfactory, we suggest the term "thalassemia" or "Mediterranean anemia."

NOTE (March 8, 1932).—Since completion of the manuscript two more cases of this type have come under observation, occurring in identical male Italian twins one of whom died and was examined at autopsy by one of us (G. H. W.). Autopsy showed this case to be practically a replica of case 1 in the preceding report. The bony changes were less conspicuous but the same heavy pigmentation of liver, pancreas, stomach, kidneys and ductless glands was found. Hypoplasia of the suprarenals was also present. The cooperation of Dr. Cyrus H. Maxwell, Jr., of Auburn enabled us to study these cases.

METHOD FOR THE CONTINUOUS INFUSION OF INFANTS

JOHN MITCHELL BRUSH, M.D.
NEW YORK

Continuous or drip infusion has been used extensively in adults. Its application to the needs of infants has been discouraged by the technical difficulties encountered. The aim is to give fluid intravenously over a period of days at a minimum rate of 240 cc. in twenty-four hours to an infant weighing 4 pounds (1.8 Kg.) or over. To do this, one must solve four cardinal problems: (1) control of the flow of fluid at a rate of 10 cc. per hour or faster; (2) regulation of the temperature of the fluid; (3) a stable connection with the patient's vein, and (4) prevention of back-flow on an increase of venous pressure.

The apparatus to be described answers all these difficulties in a new and simple manner. It requires no supervision or adjustments. Its parts are fool-proof and stable.

SOLUTION OF DIFFICULTIES

Control of Flow.—Various devices have been used. The commonest is the pinchcock, such as is employed in this apparatus but not for this purpose. Valves of varying design must require repeated adjustment to maintain a flow of not more than 1 drop every twenty seconds, especially under the hydrostatic head required for reasons to be discussed later. The flow will repeatedly stop or, and this is more to be feared, a temporary obstruction may result in the valve being left wide open, with subsequent flooding of the vascular system.

If one packs a dropper with gauze as illustrated in figure 1, fluid will continue to seep through it at a constant rate until an obstruction develops below it. The rate depends on how tightly the gauze is packed, but this is a simple adjustment made before the apparatus is sterilized. The speed of flow is varied within rather wide limits by changing the

---

Read before the Section of Pediatrics at the New York Academy of Medicine, May 14, 1931.

From the Department of Diseases of Children, College of Physicians and Surgeons, and the Babies' Hospital.

The apparatus described, complete with photograph and detailed instructions, may be obtained from J. T. Dougherty, 1150 Saint Nicholas Avenue.

height of the graduate and the fluid level in it. This checking mechanism will not stop, and fluid cannot flow beyond a very slow maximum rate.

Control of the Temperature of the Fluid.—This is generally considered to be of minor importance. Flowing at the rates with which this study is concerned, probably room temperature or 120 F. will do no harm. Undoubtedly, the patency of the vein through which a grossly abnormal fluid is passing is preserved for a longer period if its contents are at body temperature. Furthermore, one feels more assured that therapy has not produced any of several untoward symptoms that frequently arise in these very sick infants. Man-made thermal devices will cease to function and may be very dangerous. In the present problem, the application of heat must be at the point of entrance to the vein. Otherwise, because of the slow rate of flow, the fluid will cool to room temperature again.

Nature offers a heat-regulating mechanism that functions within the desired limits until therapy is no longer indicated. If about 24 inches (60.9 cm.) of a pure gum, thick-walled, small caliber tubing is coiled on the side of the leg, away from the vein, and the leg is then bandaged in cotton, without the aid of external heat, the temperature of the fluid will rise to well above 90 F. at the point of entrance to the vein; but it cannot rise too high.

Stable Connection with the Vein.—To my knowledge, only metal or glass cannulas have been used in the vein. They are relatively heavy and require careful adjustment and fixation when first introduced. They cannot follow the normal course of the vein in the tissues. They frequently angulate the vein and may cause pressure necrosis through the wall of the vessel. Motion near them is fatal to the procedure. The usual transfusion needle erodes amazingly in two days.

A soft cannula overcomes all these difficulties. The introduction of a short piece of no. 4 plain ureteral catheter (fig. 1) into an infant's vein is not a difficult technical procedure. It consists of a woven silk tube impregnated by baking with a gum distillate of linseed oil. The tip of the cannula is passed beyond the edges of the wound where it lies in the normal course of the vein and accommodates itself to changes in relationships resulting from motion such as occurs near a joint. This connection continues to function as long as the vein above remains patent.

Prevention of Back-Flow.—When a baby cries, there is a marked temporary increase in venous pressure. This forces blood back into the infusion system, which subsequently is either washed out or clots in the cannula. The latter is the usual cause of the apparatus ceasing to function. All systems using a Murphy dropper, which has an air vent,

a venous pressure manometer or one containing a large air space encounter this backing up frequently.

From figure 2, it is apparent that this apparatus is entirely closed. During normal conditions, there is a negative pressure in the air pocket below the gauze dropper because the column of water required to force fluid into the vein is less than the fluid level seen at this point. A sudden increase in venous pressure is promptly met by the height of fluid up to the level in the graduate after the air pocket has been

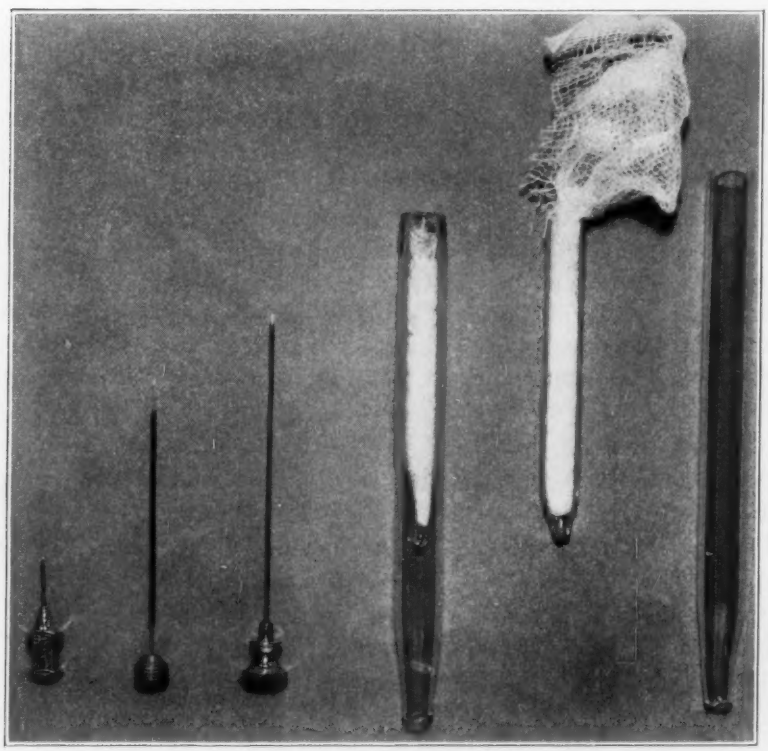


Fig. 1.—The center dropper is ready for use. The dropper and tube on the right are shown before being assembled and sealed at the upper end. The final connection with the piece of ureteral catheter shown on its stylet is completed by forcing into its lumen the short needle. The larger stylet is used to make the opening in the wall of the vein.

reduced by a pressure corresponding to the height of fluid above. Roughly calculated, a back-flow of 0.1 cc. increases the pressure from several centimeters to 1 meter if the air space is 1 cc. This reasoning followed to its logical conclusion would suggest that there will never be any back-flow if the air pocket is entirely eliminated. That is true, but probably the ability to visualize the flow is of sufficient advantage

to warrant the use of this compressible element. The other variable following changes in pressure is the capacity of the rubber tubing, but with the use of the heavy-walled variety this can be ignored. Experience shows that with a small air pocket, back-flow is a rare occurrence, and the first portion of this consists of fluid in the vein, not blood, up to the first good-sized tributary. The air pocket on the opposite side above the clamp remains constantly under the pressure of fluid above. Its size is of no moment. If one desires to visualize the flow, as small an air pocket as is compatible with this end is essential.

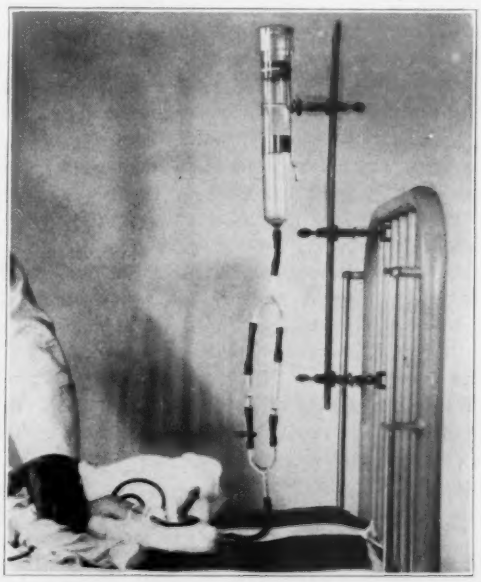


Fig. 2.—The infusion apparatus is complete except for a sterile dressing over the wound and bandaging the cotton about the leg and foot. Note the method of attachment to the bed, the fluid level in the droppers, the pinchcock entirely closed off, the coiled tubing on the far side of the leg, the catheter entering the incision under the flamed adhesive, and the bandage strip from the heel to the foot of the bed, which forms the only restraint. The droppers are now being made a standard size and the several pieces of tubing are longer.

The other details can be readily understood from the illustrations. The apparatus is clamped to an upright at the foot of the bed. From time to time, the pinchcock may be opened to allow fluid to flow as rapidly as the caliber of the several parts permits. This dropper contains no gauze. In this way, one can detect beginning occlusion of the vein. Normally this pinchcock is completely closed. This by-pass is provided essentially for emptying the system of air. The small tubing

is coiled on the lateral side of the leg to avoid pressure on the vein above the site of the attachment. A short hypodermic needle, no. 23 gage, is inserted into the free end of the catheter and makes a satisfactory connection. By no method can one avoid cutting down on the vein. Unless the vein is tied off or the needle completely fills its lumen, blood will clot about the cannula.

TECHNIC

Attention to details, which of themselves are simple, is essential. Pack the dropper with sufficient moistened gauze 3 inches (7.6 cm.) wide to deliver approximately the flow desired, be it 10, 25 or 75 cc. per hour. This is tested by setting up the apparatus on a ring stand. All parts of the system, including catheter and stylets, are boiled for ten minutes. Clamp the holder to an upright at the foot of the bed. Place the small tubing with its Luer tip in a bowl and cover with a sterile towel. Place the graduate in its holder and close the pinchcock. Fill the graduate with fluid and put the cover in place. The routine mixture consists of two parts of 5 per cent dextrose and one part of physiologic solution of sodium chloride. One must bear in mind the tendency of even fresh dextrose solutions to cause thrombosis. This causes no trouble other than stopping the infusion.

Expel the air above the droppers by compressing the tubing. After raising the lower end of the droppers just above the horizontal position, allow the gauze dropper almost to fill the space below its tip with fluid. Open the pinchcock and allow the other dropper tube to fill partially. Pinch the tubing immediately below the droppers and drop to just below the horizontal position. This allows the trapped air to rise about the dropper points. If the proper amount of air has been trapped, release the pressure on the tubing allowing the fluid to fill the Y piece to its junction, when it can be readily made to fill the opposite side. Then, and not until then, return both droppers to their normal vertical position. Empty the system of air in the usual manner. The manipulation just described requires but little practice.

Pass a strip of bandage from the bed frame on each side over the mattress about 1 foot (30.5 cm.) from the end of the bed. Tie the bandage at the point that will allow its free ends to be fastened about the ankle opposite to the leg chosen. Pass another strip of bandage from the upright supporting the apparatus to this cross-piece. Fasten the infant's foot to this vertical strip with adhesive. Evert the leg and fix by passing adhesive over the metatarsal arch and under the cross-restraint.

The vein used is the great saphenous vein at any point from the ankle to the midthigh. The site of election in the small infant is the midleg, where the vein is readily found at the posterior border of the medial aspect of the tibia. Deliver the vein through the wound and clean it in the usual manner. Pass a silk ligature under it. Introduce the larger stylet into the lumen and withdraw it. Cut a bevel end on the catheter and assemble with the smaller stylet. Moisten the end with a solution of procaine hydrochloride or saline solution. Pass the point of the stylet through the hole in the wall of the vein. Maintain gentle pressure to force the catheter into the vein. After about one minute, the wall of the vein will relax and the catheter will slip into its lumen even though the vein appears to be one-half the diameter of the cannula. Withdraw the stylet part way and pass the catheter up the vein until its tip is beyond the margins of the wound. Introduce the hypodermic needle into the free end of the cannula as far as it will readily go.

Then the final connection is made with the hose tip. Open the pinchcock to wash out blood that has come back into the cannula. Tie the ligature about the vein and catheter with a single knot. Cut one end very close. This obviates the necessity of opening the wound at the termination of the procedure. Close the wound with flamed adhesive. Stabilize the connections with adhesive. Place a pad of cotton under the leg. The small tubing passes under the ankle and is coiled on the lateral side of the leg. Strap the connection with the larger tubing to the ankle. Cut away the cross-restraint. Bandage the entire leg and foot in the cotton. Close the pinchcock. The rate of flow can be more than doubled or cut in half by raising or lowering the graduate and the fluid level in it. This procedure should require not more than one hour to complete.

COMMENT

Fluid must be added every two to six hours, depending on the rate of flow. No other care is required. The gauze checking mechanism will not stop, nor can it allow fluid to flow too fast. The heating mechanism will continue to function as long as the patient survives. A flexible tube lies in the vein and cannot and need not be adjusted. Backflow is prevented by the potential hydrostatic pressure always present. The duration of the infusion depends on the persisting patency of the vein, which is usually well over three days, or this form of therapy can be terminated by choice. The baby can be lifted or turned on its abdomen. Any nursing care or examination may be carried on which allows the foot to remain within 12 inches of the end of the bed.

I am not concerned here with the clinical indications, the results obtained or the modifications of the chemical constituents of the blood produced by these infusions. This form of therapy has been used over forty times in the wards. The entire amount of fluid required by the patient may be given by this method at a physiologic rate over a period of days without disturbing him any more than for a single infusion.

SUMMARY

1. A method for the continuous infusion of infants is presented.

2. It embodies new principles which obviate the four primary difficulties encountered in this procedure.

3. No supervision or adjustment is necessary, thereby introducing a new element of simplicity and safety.

21 East Eighty-Seventh Street.

DISEASE OF THE GALLBLADDER IN CHILDREN

ALBERT H. MONTGOMERY, M.D.
CHICAGO

It is well recognized that there are certain pathologic conditions that affect children with such rarity that their occurrence is regarded as a medical curiosity. Disease of the gallbladder has been placed in this category by most physicians and looked on as an affliction to which children are fortunately immune. The opinion of clinicians has been fostered by the presentation of this subject in most of the textbooks on pediatrics and surgery in children, in which the authors either omit any mention of the gallbladder or merely call attention in a few lines to the rarity of disease of that organ in children. Their attitude is probably due to the small number of cases that have been reported in the literature. Synder,[1] in 1925, called attention to the fact that, following the case reported by Gibson in 1722, Kellogg[2] in 1923 was able to collect only sixty-four cases, exclusive of eighteen reported by Reid and Montgomery,[3] or a total of eighty-two cases in the period of two hundred years. In the same year, 1923, Porter,[4] writing in Abt's "Pediatrics," said, "Pathological involvement of the gall-bladder in children is practically unknown." Fraser,[5] in his text written in 1926, made no mention of surgical intervention on the gallbladder. Melchior[6] referred to the monograph of Gohrbundt, Karger and Bergman published in 1928, in which they said that these cases are rarities of no practical importance which hardly ever come to operation. In striking contrast is the report of Potter[7] in 1928, in which he presented 226 cases collected from the

---

Read before the Chicago Surgical Society, April 3, 1931.

1. Synder, C. C.: Cholecystitis and Cholelithiasis in Children, J. A. M. A. **85**:31 (July 4) 1925.

2. Kellogg, E. L.: Gallbladder Disease in Children, Ann. Surg. **77**:587 (May) 1923.

3. Reid, M. R., and Montgomery, J. C.: Acute Cholecystitis in Children as a Complication of Typhoid, Bull. Johns Hopkins Hosp. **31**:7 (Jan.) 1920.

4. Porter, Langley, in Abt, J. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1924.

5. Fraser, John: Surgery of Childhood, New York, William Wood & Company, 1926.

6. Melchior, E.: Cholecystitis in Childhood, Beitr. z. klin. Chir. **150**:298 and 300, 1930.

7. Potter, A. H.: Gallbladder Disease in Young Subjects, Surg., Gynec. & Obst. **46**:795 (June) 1928.

literature up to August, 1927. All of these patients were under 15 years of age, and the diagnosis was proved in every one by operation or autopsy. As this large series does not contain an indefinite number of cases that were probably observed but not reported, the incidence of disease of the gallbladder is undoubtedly greater than has hitherto been believed, and the impression of the rarity of this condition must undergo revision upward. Since the report of Potter, cases have been reported by Beals [8] in this country, by Vollmer,[9] Pop and Muresan [10] and Melchior in Germany.

My attention was drawn to this subject by a patient with the following history:

REPORT OF A CASE

CASE 1.—*History.*—H. McK., a white boy, aged 7 years, entered the Children's Memorial Hospital on Nov. 18, 1930, because of attacks of abdominal pain. His mother stated that eight weeks before, the boy was suddenly atacked with cramp-like pains in the lower part of the abdomen, localized apparently in the midline about half way between the umbilicus and the pubis. The pains, which were intermittent, lasted from five to ten minutes, and were severe enough to cause the child to double up. Since the onset, the boy had had daily attacks of this character, usually accompanied by a temperature of from 100 to 101 F. The attacks occurred at irregular times during the day, and seemed to have no relation to the taking of food. The bowels had always been regular, but the child's appetite was only fair.

Two years previous to admission the boy had had measles and scarlet fever, and he had mumps one year ago. He was quite susceptible to colds and sore throats, but otherwise his general health had been satisfactory.

Examination.—Aside from enlarged, infected tonsils and a few small cervical lymph glands, nothing abnormal was found on physical examination. No masses, rigidity or tenderness were found on abdominal palpation. Laboratory examination of the stools, urine and blood gave essentially negative results.

Roentgen examination was made by Dr. H. Rudisill, Jr. Fluoroscopically, with a barium enema, the colon showed nothing abnormal, but a roentgenogram showed an oval area of calcium density overlying the twelfth rib on the right side. Another roentgenogram taken six days later with the tube at an angle toward the feet showed the calcified area about 1 inch (2.5 cm.) below the twelfth rib. In that position it could be seen well, and showed two small areas of decreased density, suggesting the appearance frequently seen in gallbladder disease in which non-opaque stones are embedded in a calcium carbonate matrix. The roentgenogram taken in the latter position showed the calcification to be about 2 inches (5 cm.) anterior to the second lumbar vertebra, which seemed to be too far anteriorly for a kidney stone and too far posteriorly for a gallbladder calculus.

The following day pyelograms were made after the injection of 75 cc. of iopax intravenously. Anteroposterior films taken five and twenty-five minutes after injection showed faint but normal right and left pyelograms. The calcified mass was

8. Beals, J. A.: Cholecystitis and Cholelithiasis in Children, South. M. J. **21**: 666 (Aug.) 1928.

9. Vollmer, H.: Cholecystitis in Children, Ztschr. f. Kinderh. **49**:200, 1930.

10. Pop, A., and Muresan, E.: Ztschr. f. Chir. **5**:267, 1930.

just above the superior right major calyx and appeared within the kidney shadow. A lateral view, however, showed this calcification to be at least 3 inches (7.6 cm.) anterior to the pyelograms and therefore definitely not in the right kidney. Two days later films were taken after the oral administration of gallbladder dye. Three films taken eight hours after the dye was given failed to show a shadow of the gallbladder. It was noticed, however, that the oval calcification had changed its axis, thus probably ruling out the diagnosis of a calcified gland. A few days later the gallbladder dye was given intravenously, and roentgenograms were taken in the anteroposterior and lateral positions four and eight hours after administration. They showed the calcified mass in the dependent portion of the faintly visualized gallbladder, which seemed rather enlarged for a small child. Two films taken twenty-four hours after the administration of the dye and after the child had eaten showed no trace of the shadow of the gallbladder.

From this study, Dr. Rudisill felt justified in making a definite diagnosis of a calcified stone in the gallbladder.

Opened gallbladder in case 1, showing kissing ulcers and mulberry gallstone.

Operation.—Under ether anesthesia the abdomen was opened by an upper right rectus incision on Jan. 17, 1931. The gallbladder was somewhat gray and contained a stone about the size of a large grapefruit seed lying free in the fundus. The appendix was then examined, but showed no abnormality. The gallbladder was dissected free from the liver, the cystic duct clamped off close to the common duct, and the organ removed intact. The appendix was amputated in the usual manner, and the abdomen closed after one cigaret drain was placed in the bed of the gallbladder.

Postoperative convalescence was uneventful, and the child was discharged in good condition, with the wound healed sixteen days after operation.

Laboratory examinations of the specimens were made by Dr. William Hibbs. Cultures of the gallbladder contents were sterile after forty-eight hours. When opened, the gallbladder was found to contain some dark, viscid bile and one mulberry-like gallstone. At the site of the gallstone in the fundus two kissing ulcers were present (accompanying illustration). Otherwise the lining and wall of the gallbladder appeared to be normal. Histologic sections, however, showed a

subacute inflammation of the wall, with acute ulcerative inflammation at the site of the gallstone ulcer. Grossly and histologically, the appendix showed nothing abnormal.

Chemical analysis of the stone, made in the University of Chicago laboratories, was as follows: weight, 0.15 Gm.; calcium, 33 mg., and phosphorous, 5.2 mg. per hundred milligrams of stone. Qualitative tests showed the presence of a trace of cholesterol and of the bile pigments.

The high percentage of calcium was, of course, in keeping with the outstanding shadow seen in the roentgenograms. The presence of only a trace of cholesterol might in this instance speak against cholesteremia as a possible etiologic factor.

COMMENT

Infection has always been looked on as a pronounced cause of the production of cholecystitis. Reid and Montgomery, Deaver [11] and others have reported cases due to typhoid organisms. However, with the modern sanitary control of typhoid fever, the number of cases in children due to this bacillus will be very small. On the other hand, Potter pointed out that many patients have a preceding history of influenza and scarlet fever, with a probable bacteremia and localization in the gallbladder. He thinks that the infections of childhood play an important but generally unrecognized rôle in the etiology of this condition. Farr emphasized the association with appendiceal infections, and his opinion is fortified by a number of cases that occurred with, or shortly after, appendicitis. Also infections of the digestive tract, especially in young children, are frequent and must be considered as a possible etiologic factor. Melchior reported a case that seems to show a definite family tendency to cholecystitis. Vollmer reported a case that followed a blow to the abdomen with a football. Sex, which plays such an important part in cholecystitis in adults, is apparently not such a factor in children. Almost half of Potter's cases, in which the sex was known, occurred in males.

The frequency of gallstones in children is probably greater than is generally supposed. Many clinicians think that they do not occur in the first decade, and that they are extremely rare in the second decade. Gallstones, however, have been found at all ages, even in a 6 months fetus. They were present in 140 of the 226 patients in Potter's series.

The clinical picture presented by most children with disease of the gallbladder is that of an acute abdominal infection. Pain, tenderness, vomiting, rigidity, a high temperature and leukocytosis are exhibited. The pain, however, is usually located in the region of the umbilicus and does not radiate to the back or shoulder. Some patients may show a variable degree of jaundice, but many do not. Occasionally, the

11. Deaver, H. C.: Cholecystitis Following Typhoid Fever in Childhood, Ann. Surg. **69**:534, 1919.

gallbladder may be enlarged and palpable. The clinical picture of an acute condition is illustrated by the following case:

CASE 2.—*History.*—J. C., a white boy, aged 10 years, entered the hospital on June 27, 1923. The night before he had been awakened by severe abdominal pain and an attack of vomiting. The pain was sharp and cramplike; it was generalized over the abdomen, but was more severe in the upper portion. It had been present almost continuously since the onset. There was no history of any dietary indiscretion that might have caused the present illness, and, except for an attack of measles over two years before, his health had been very good.

Examination.—When he was examined at the hospital, about fifteen hours after the onset, there were definite tenderness and abdominal rigidity on the right side, most marked at the level of the umbilicus or just above it. The temperature was 101.5 F. and the pulse rate, 100. Examination of the urine showed nothing abnormal, but a blood count showed leukocytosis with a cell count of 14,000. A diagnosis of acute appendicitis was made, and immediate operation was advised.

Operation.—Under ether anesthesia the abdomen was opened by a right rectus incision instead of by the usual McBurney incision, as the point of maximum tenderness was at the level of the navel. The appendix was found lying in the right iliac fossa and showed no evidences of any pathologic changes. The gallbladder was then palpated, and it seemed larger and firmer than normal. When explored by slightly enlarging the incision, it was found to be dark red and attached to the omentum by fine adhesions. The appendix was removed and the gallbladder drained by the usual cholecystostomy. The gallbladder was filled with very dark, thick bile, but no stones were present.

The child made an uneventful recovery and left the hospital twenty-three days after operation with a small draining fistula which closed in about ten days.

Cultures made from the bile showed the colon bacillus to be the infecting agent. Most probably it had come from the bowel, either as an ascending infection or by way of the portal system.

CASE 3.—*History.*—An Italian boy, aged 6 years, whom I saw in consultation, had been seized with a generalized cramplike abdominal pain of severe degree accompanied by vomiting. In the course of ten hours the pain had become localized to the right side along the outer edge of the rectus muscle. When I saw the boy with his physician about fifteen hours after the onset, he appeared to be in considerable pain. He had a grunting respiration and held his abdominal muscles rigidly fixed. On examination, a point of marked tenderness was found on the right side just above the level of the navel and lateral to the rectus muscle. The pain did not seem to radiate.

Examination.—His temperature was 101 F., and the white blood count was 17,000. Nothing abnormal was found in the urine. On physical examination the chest was normal, and nothing was found except the localized tenderness and rigidity in the right side of the abdomen. Because of the grunting type of respiration, pneumonia or pleurisy was suspected but could not be confirmed by physical examination. The possibility of disease of the gallbladder was considered but discarded, because of its rarity in children, in favor of a diagnosis of acute inflammation in a high-lying appendix.

Operation.—When the abdomen was opened, the appendix appeared to be quite normal, but the gallbladder was red, thickened and friable. Because of the apparent severity of the infection, it was suggested to the surgeon that the operation be

limited to a simple drainage of the gallbladder. He decided, however, to remove the organ, and did so with some difficulty because of its friability.

The boy died forty-eight hours later of fulminating general peritonitis. Postmortem examination was not permitted, but cultures of the gallbladder showed a hemolytic streptococcus as the offending organism.

COMMENT

The chronic cases are not nearly so frequent as the acute cases if one may judge from the number reported, but I believe with Farr [12] that a large number are not recognized. These patients often give a history of attacks of abdominal colic lasting from a few minutes to several hours, usually associated with nausea and vomiting. Tenderness, rigidity, leukocytosis, a high temperature and jaundice are absent unless the picture changes to the acute type. Between attacks of colic there may be some symptoms of indigestion.

Like many conditions in medicine, the diagnosis can often be made if the clinicians will cease thinking of cholecystitis as an extreme rarity in children and keep it in mind as a possibility in cases of acute abdominal pain. Farr has pointed out that practically all the cases on record have been reported by surgeons and not by pediatricians. As the pain is usually localized to the abdomen without radiation, and as a high-lying appendix is not infrequent in children, many of these patients will undoubtedly be operated on under the diagnosis of appendicitis. The presence of distention, with pain, vomiting and constipation, may suggest acute intestinal obstruction. When a mass is palpable, intussusception may be considered, but the absence of blood in the stools will exclude that condition. A peptic ulcer with perforation was simulated in the case reported by Pop and Muresan. Renal colic can usually be excluded by urinalysis.

In chronic cases in which an operation is often done as a last resort under the indefinite diagnosis of chronic appendicitis, I wish to suggest the use of cholecystograms as a diagnostic aid. Dr. Evarts Graham has stated that he has been able to diagnose several of these puzzling cases by the use of his dye test. In his book published with Cole, Copher and Moore [13] it was stated:

> Until recent years cholecystitis in the young was considered to be a rare disease. Although still uncommon, it is our opinion that if cholecystographic examination is carried out more frequently in children more cases of cholecystitis will be recognized in childhood. We feel also that probably many of the cases, first recognized later in life had their origin in childhood, possibly as cases of supposed

12. Farr, C. E.: Cholecystitis and Cholelithiasis in Children, Arch. Pediat. **39**:574 (Sept.) 1922.

13. Graham, E. A.; Cole, W. H.; Copher, G. A., and Moore, S.: Disease of the Gall Bladder and Bile Ducts, Philadelphia, Lea & Febiger, 1928.

catarrhal icterus, or of acute indigestion of some sort. In our records at the St. Louis Children's Hospital during the past ten years there were found 8 cases of cholecystitis occurring between the ages of one and one-half and fifteen years, practically all of which were confirmed by operation or autopsy. All the cases subjected to operation were found to have large distended gall-bladders which were reddened and inflamed, but which showed very few adhesions and very little thickening of the wall itself.

From a fairly careful review of the literature it would seem that the first case reported was unique in that the presence of the stone was definitely diagnosed and demonstrated in the gallbladder previous to operation.

The pathologic changes that occur in the gallbladder in children do not differ particularly from those that occur in the gallbladder in adults, and so the treatment employed is carried out along the same surgical principles. Children do not have the same power as adults to wall off infection. Therefore, in the acute cases it is probably wiser not to attempt conservative treatment in the hope that the acute inflammatory process will subside, but to use surgical treatment at once.

The experience derived from these cases would seem to suggest that whenever a surgeon who is operating on a child for acute appendicitis finds that the appendix shows little or nothing abnormal, the gallbladder should be carefully examined. It may show pathologic evidence which will indicate the correct diagnosis and treatment.

122 South Michigan Avenue.

Case Reports

PAROXYSMAL HEMOGLOBINURIA CURED BY INOCULATION OF SPIROCHAETA MORSUS MURIS

S. INAMORI
MUKDEN, CHINA

In spite of the general conception that the etiology of paroxysmal hemoglobinuria lies in syphilis, no applicable treatment has yet been discovered. It is obvious that some antisyphilitic remedies, e. g., arsphenamine, mercury and potassium iodide, exert a curative action on hemoglobinuria to a certain extent, but several years of continuous administration are required, and even then complete convalescence may not be assured. In the clinic of the Manchuria Medical College, a few years ago, a child recovered from paroxysmal hemoglobinuria although the Wassermann test remained positive after more than a year's treatment by inunctions of mercurial ointment, injections of neoarsphenamine and oral antisyphilitic therapy.

Recently, inoculation with Plasmodium malariae has been in common use in the treatment for syphilitic diseases of the nervous system, and the same method has been adopted in the treatment for hemoglobinuria, but to the present time there is no literature regarding the success of the treatment. Moreover, there is difficulty in keeping the virus for ready use, and malaria brought about by the inoculation may cause a patient to suffer severely, especially if it be a child.

Since Solomon's report in 1926, inoculation with Spirochaeta morsus muris, which is a causative agent of rat-bite fever, has been generally practiced, as it gives good results in the treatment for syphilitic diseases of the nervous system. There is no trouble in transferring the spirochetes from one mouse to another. Thus the treatment for syphilis has become much more effective than before, but no research worker has ever tried spirochetes in the treatment for hemoglobinuria. Lately, my associates and I had a successful result in such a case.

REPORT OF A CASE

History.—A boy, aged 7 years and 8 months, was admitted to the clinic on Feb. 7, 1930. Both parents were healthy, and he had had four brothers, one of whom had died of phthisis pulmonum. The mother had had a spontaneous abor-

From the Department of Pediatrics (Prof. I. Inaba), Manchuria Medical College.

tion in the third month of pregnancy. The boy was the third child, and was born at full term. When he was 3 years old, he suffered from exudative pleurisy.

The patient had been complaining of cyanosis and edema on the extremities and ear-lobes, accompanied by fever and palpitation, and he had passed a large amount of dark red urine every winter for about three years. The cyanosis and edema disappeared whenever he took a warm bath.

Examination.—The patient was normal in nutrition and structure, but was very pale. The ear-lobes were reddish purple. The pulse rate was normal. There were a few lymph nodes as large as a pea on both sides of the neck. The cubital lymph nodes on both arms were the size of a grain of rice. The temperature and respiration were normal. The child weighed 17.55 Kg. At the apex of the heart and pulmonary ostium the systolic sound was not clear and the diastolic pulmonary sound was accentuated. No pathologic sign was found in the chest. The abdomen was normal. The liver was palpable at 1 cm. beneath the border of the ribs. The spleen was not palpable. No edema was present in any part of the body. The knee reflexes were normal. The urine was reddish brown and turbid with no albumin or urobilinogen and hemoglobin +. The Wassermann and the Meinicke reactions of the blood were positive.

Course.—February 10: Inunctions of mercurial ointment were commenced.

February 11: On the left instep, a slight, and on the ear-lobes a severe, edematous cyanotic change occurred, which disappeared after about nine hours. The urine was dark red.

March 29: Inunctions had been administered twenty-four times. The test of chilling of the blood by the Donath and Landsteiner method, using the serum of the patient mixed with his own blood corpuscles, gave strong positive results.

April 2: A chilling test was performed by immersion of the extremities in cold water (4 C.) for half an hour. An hour after the test, dark red urine containing hemoglobin was passed.

April 4: The Wassermann reaction was ++++; the Murata reaction was +++, and the Meinicke reaction was +.

April 14: The patient was inoculated subcutaneously with 5 drops of blood taken from a guinea-pig that had been infected by rat-bite fever mixed with 0.5 cc. of physiologic solution of sodium chloride. He weighed 17.6 Kg.

April 21: The temperature rose to 37.8 C. (100 F.). The inoculated area was slightly painful on pressure, but there was no induration or redness. The patient complained of headache.

April 22: The highest temperature was 39 C. (102 F.). Since the evening of April 21, he had vomited twice.

April 23: The fever continued. The inoculated area was swollen and painful. There was no vomiting. The child weighed 17 Kg. No lymph node was palpable as may occur after an inoculation.

April 30: The inflammation of the inoculated area disappeared, and the patient felt no pain there on pressure. The temperature was 39 C. He weighed 16.44 Kg.

May 5: An intravenous injection of 0.03 Gm. of neoarsphenamine was given.

May 6: The patient was prostrated and had a poor appetite. An intravenous injection of 0.25 Gm. of neoarsphenamine was given.

May 7: He complained of headache and sleeplessness.

May 8: The temperature became normal.

May 10: An injection of 0.3 Gm. of neoarsphenamine was given.

May 15: An injection of 0.3 Gm. of neoarsphenamine was given.

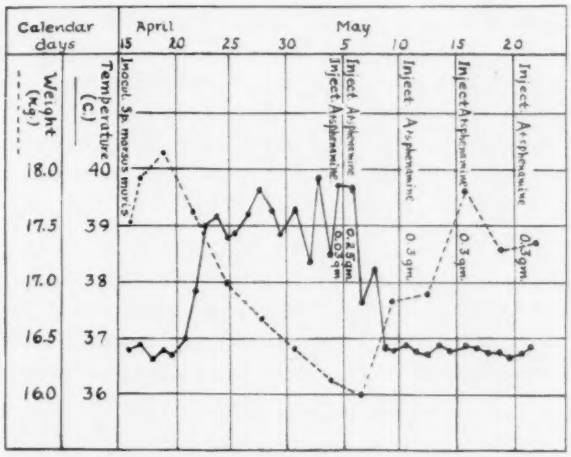
May 20: The Wassermann reaction was +++, the Murata reaction +++, and the Meinicke reaction +.

May 21: An injection of 0.3 Gm. of neoarsphenamine was given.

May 22: Fifteen minutes after a chilling test of the extremities in cold water (4 C.) the patient passed urine of a dark red wine color. The pulse rate and the heart were normal. The urine showed: no acid; albumin, +; hemoglobin, +++; no urobilin, urobilinogen or sediment.

May 23: Since May 17, the child's complexion had been good; he felt vigorous and had a good appetite. His heart was normal and he was discharged from the hospital (chart).

Feb. 20, 1931: The boy visited the clinic to report that he had received no treatment since he had been discharged. Since November of the previous year, he had skated at a temperature of from 5 to 10 C. below zero, for several hours every day, but no cyanosis had occurred on the ear-lobes or on the extremities, nor did he pass dark red urine.



Curves showing body weight and temperature.

Examination.—The patient had a good complexion and was well nourished. The cubital lymph nodes on both arms were the size of a grain of rice. The throat, heart and lungs were normal. The liver was straight at the costal arch. The spleen was not palpable. The boy weighed 19.9 Kg. The test of the blood by the Donath and Landsteiner methods and a chilling test of the extremities in ice water (from 2 to 3 C.) for one and one-half hours gave negative results.

The Wassamann reaction was ++; the Murata reaction was +, and the Meinicke reaction was negative. Thirty minutes after the commencement of the chilling test, the temperature rose to 37.4 C. (99.3 F.), and then dropped gradually. The urine passed three times in two hours during the test and once afterward contained no hemoglobin.

COMMENT

The patient had complained of paroxysmal hemoglobinuria for three winters. During the first period of the treatment, he was given inunctions of mercurial ointment for about forty-five days, and in the following thirty days he was subjected to an inoculation with Spirochaeta

morsus-muris and five injections of neoarsphenamine. Thus he became totally free from hemoglobinuria as a result of treatment during seventy-five days after he came under our care. As it is generally recognized, inunctions of mercurial ointment for the duration of only forty-five days bring about no remarkable effect; therefore, the essential treatment was the inoculation with the virus of rat-bite fever, and the duration of this treatment was only thirty days.

Just before his discharge, the patient gave a positive reaction to the chilling test, thus showing that his recovery was incomplete; but according to the literature on this problem, treatment with the spirochetes does not yield a definite effect immediately, although it does so a month or two later. For the same reason, the approximate day of his convalescence cannot be ascertained; however, it is certain that he had recovered some time before November, six months after his discharge, as he no longer complained of hemoglobinuria, although he had been skating several hours every day at a temperature some degrees below zero. When he was examined six months after discharge, he was not yet free from syphilis, judging from the fact that he showed a positive reaction to the Wassermann test, but he had recovered from hemoglobinuria, as he gave negative reactions to the Donath and Landsteiner and the chilling tests.

SUMMARY

A patient who had been suffering from paroxysmal hemoglobinuria for three years was cured after having been kept in a febrile condition for sixteen days by an inoculation with Spirochaeta morsus-muris.

AGLOSSIA CONGENITA

REPORT OF A CASE OF THE CONDITION COMBINED WITH OTHER CONGENITAL MALFORMATIONS

ROBERT ROSENTHAL, M.D.
ST. PAUL

Congenital absence of the tongue is extremely rare; only a few cases have been reported in living children. Usually the tongue has been found to be absent in cases of gross underdevelopment or maldevelopment of the first visceral arches, especially in cases of congenital agnathia or micrognathia.[1]

To understand the etiology one has to know some facts about the development of the tongue. The tongue has its origin in the pharynx and grows forward into the floor of the mouth. It begins with a swelling on the floor of the pharynx between the first and second visceral arches, the tuberculum impar, which is present before the embryonal age of 4 weeks. The part formed from it is only a small part of the tongue, that just in front of the foramen caecum. The anterior portion develops from the so-called lateral tongue swellings of the first or mandibular arch, from which arch the mandible also develops (the right and left lingual buds appear in the fifth week). These two swellings later fuse in front of and with the tuberculum impar and grow forward to form the greater part of the tongue. This fusion is completed after the seventh week, as in the seventh week the tip of the tongue is still bifid. The posterior part, the radix linguae, originates from a medial swelling, the cupola, at the base of the second and third arches, posteriorly to the tuberculum impar; this part is the one back of the v-shaped row of the papillae circumvallatae. The union of the anterior and posterior parts is later marked by the sulcus terminalis. The muscles are probably derived from the mesenchyma of the floor of the mouth.[2]

Underdevelopment and total absence of the tongue are due to nondevelopment of one or more of the aforementioned parts of the embryonal tongue. Incomplete fusion is a cause of deformities, the

1. Aschoff: Missbildung der Zunge bei Agnathie, Verhandl. d. deutsch. path. Gesellsch., 1901, p. 176. Swoboda, N.: Micrognathia, Allg. Wien. med. Ztg., 1904, p. 94.

2. Keith, Arthur: Human Embryology and Morphology, ed. 4, London, E. Arnold, 1921. Dodds, G. S.: The Essentials of Human Embryology, New York, John Wiley & Sons, 1929. Shumway, Waldo: Introduction to Vertebrate Embryology, New York, John Wiley & Sons, 1930.

most common of which is the bifid tongue, or lingua bipartita, due to the lack of fusion of the lateral tongue swellings. In Kettner's case a broad band was found at birth running across the mouth between the tongue and the palate, and he expressed the belief that in his case amniotic amputation should be considered.

Therapy is of no avail. Children with this condition usually learn to eat slowly, but later they become quite adept in using whatever rudiments they have in their mouths and, in the case of solid food, helping with the finger to push it along toward the pharynx. Artificial tongues did not prove practicable, even in adults. The speech, which is very poor in most cases during the first few years, may improve considerably when the child learns to use other muscles in substitution for the missing tongue.

After a very careful search of the literature I was able to collect only three cases. Many of the reported cases of "absence of the tongue," even in children, proved to be aglossia due to loss of the tongue during life, usually due to gangrene following smallpox.

The first case is that reported by de Jussieu.[3] He described a case in a 15 year old girl who had only a tiny wartlike elevation in place of a tongue; certain rudiments of musculature were present, as some contractions could be felt. The girl talked quite plainly, although the author did not go into detail as to which letters could not be properly pronounced. The sense of taste was not impaired, and the patient was able to chew with some difficulty. In the absence of the tongue she used the finger to push the food between the teeth. She swallowed fluids fairly well, but she had to be careful to take only small amounts at a time, and she had to bend forward. Nothing is said as to whether the child had been able to nurse at the breast. In the more recent literature this seems to be the only case referred to as an authentic case of congenital aglossia.[4]

---

3. de Jussieu, M.: Observation sur la manière dont une fille sans langue s'acquitte des fonctions qui dependent de cet organe, Hist. Acad. roy. d. sc., Par. 1718, 1719, mém. 6 to 14. (This article was republished in several European periodicals, the last time as late as 1770.) Meyer, M. W., in his article: Ueber die angeborenen Fehler der Zunge und die dadurch bedingte Hinderung des Saugens (J. f. Kinderkr. **13**:328, 1849) stated that the Portuguese physician, Dr. Somarive, published a description of the same case in a special pamphlet.

4. Gould, G. M., and Pyle, W. L.: Anomalies and Curiosities of Medicine, Philadelphia, P. Blakiston's Son & Company, 1897. Birnbaum, R.: A Clinical Manual of Malformations and Congenital Diseases of the Foetus, translated by G. Blacker, London, J. & A. Churchill, 1912. Birnbaum said that Tillmans had reported a case (of congenital absence of the tongue) from the French literature. This is without doubt the case of de Jussieu. Thomas B. Cooley, in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1925: "Aglossia: There is at least one authentic case of congenital absence of the tongue, that of Jussieu."

The second case appeared about one hundred years later, and was reported by Dr. Spiller, a physician of Pennsylvania, in the early part of the nineteenth century.[5] This patient showed in place of the tongue a shallow elevation across the mouth in the region of the root of the tongue. When the child cried or when this region was touched a contraction occurred, and this rudiment appeared like a ridge. There was an almost entire absence of the soft palate, except for two lateral rudiments. The infant had considerable trouble in nursing; one could see the cheeks work like a bellows. The fact that the milk frequently regurgitated through the nose was probably due to the defect of the palate.

The third case, which occurred rather recently, was reported by Kettner.[6] It was perhaps not a case of aglossia in the strictest sense, but the defect was so great that the case can be included in this group. Kettner described a boy who showed practically complete absence of the tongue; there was only a small mass, the size of a quarter, near the pharynx. This mass was triangular and pointed in front, at the site where normally the body of the tongue should start. There were two parallel ridges on the floor of the mouth extending anteroposteriorly, which showed good mobility; they could be stretched so as to almost fill the space between the teeth. They represented the sublingual ridges, and no doubt contained rudiments of the styloglossus and the hyoglossus. They took on the functions of the tongue, pressed the food between the teeth and made a furrow during swallowing to allow fluids to flow toward the pharynx. This child was able to talk, and he could pronounce all the vowels and most of the consonants, especially the ones that do not depend on the tongue for pronunciation. Besides this anomaly there were a complete cleft of the palate and severe anomalies of both feet: of the right foot only the heel and a soft ridge where the metatarsus should be were preserved, and the left foot was entirely absent except for a trace of the heel. There were also anomalies of the hands: both index and middle fingers were absent, and all the other fingers were deformed in some way, with the exception of the right little finger.

I wish to add another case to this small group. The case herein reported is similar to that of Kettner on account of the presence of multiple deformities besides the aglossia.

---

5. Quoted from Meyer, M. W. (footnote 3, second reference). Meyer presented a complete account of the case. He gives as reference the "*Philadelphia Medical Examiner* of the year 1816." This is evidently incorrect as this journal did not appear until 1838 and its indexes fail to show such an article by Dr. Spiller.

6. Kettner: Kongenitaler Zungendefekt, Deutsche med. Wchnschr. **23**:532, 1907.

REPORT OF A CASE

The patient was a girl, 3 years and 3 months old, whose parents were well. There were no congenital anomalies on either side of the family, and the two older brothers of the patient were perfectly normal. The mother's pregnancy and delivery were normal. The child was unable to nurse at the breast, but had to be fed with a long, soft nipple. The patient was rather small, and a fairly marked retrusion of the lower jaw combined with a narrow chin gave the face a peculiar

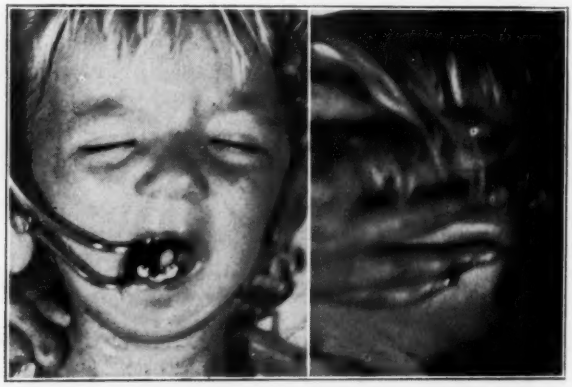


Fig. 1.—On the left, a front view of the patient is shown. Note the hypertrophic left sublingual ridge simulating a rudimentary tongue. The real tongue rudiment is not visible. Note the absence of lower incisors. On the right, a lateral view is shown. Note the retrusion of the lower jaw.

Fig. 2.—Photograph of the right hand.

appearance (fig. 1). The child presented multiple deformities of the mouth and the extremities.

The right hand (fig. 2) had only one finger, which appeared to be the thumb. A roentgenogram revealed that the distal epiphyses of the forearm were normal; the ossification centers of the os magnum and os unciforme were much smaller than normal, as were also those of the semilunar and scaphoid bones. There was a rudimentary fifth metacarpal. Two bones in the thumb represented either a rudimentary metacarpal and a rudimentary first phalanx or two rudimentary phalanges.

The left hand (fig. 3) showed a perfectly normal wrist. The last three fingers were normal; the thumb showed a first phalanx that was broader and shorter than normal and also some underdevelopment of the end-phalanx. The index finger had a rudimentary second phalanx; the end-phalanx was absent.

The right foot (figs. 4 and 5) had a normal ankle; the calcaneus and talus also appeared normal. The other tarsal bones, however, were absent, as were also all of the metatarsal bones. There was only one toe, the large one; in this toe only one bone was present, apparently a rudimentary first phalanx. The left foot was perfectly normal. The child was not incapacitated by the aforementioned deformities; she walked like a perfectly normal child, and used both hands with great dexterity.

The face was deformed, owing to a marked retrusion of the lower jaw, a slight protrusion of the upper jaw (intermaxillary region) and a narrow chin, which gave the face a tendency toward a so-called "bird face" appearance, which is

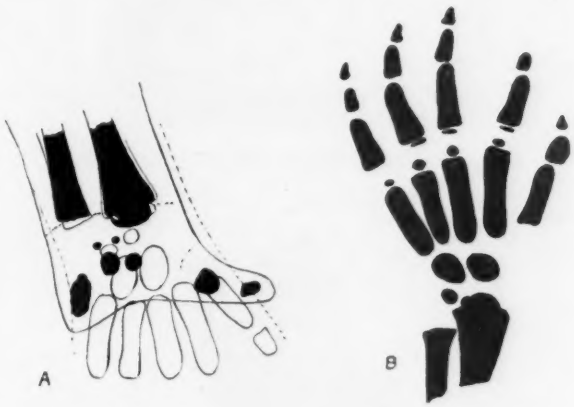


Fig. 3.—*A*, graphic representation of roentgenogram of patient's right hand (in black) superimposed on a drawing of a normal wrist. *B*, graphic representation of roentgenogram of patient's left hand.

usually due to an underdevelopment of the lower jaw (fig. 1). There was a rudimentary cleft in the lower lip (median notch). All of the incisors in the lower jaw were missing; the space between the left and the right half of the mandible was very narrow (fig. 1). A roentgenogram revealed an unerupted tooth in the anterior portion of the mandible, but it was difficult to ascertain whether it was a retained incisor or a permanent canine or bicuspid. The first molars and the permanent upper teeth were plainly visible in the roentgenogram.

The tongue was practically absent. There was only a tiny rudiment where the musculus genioglossus normally inserts on the lower jaw, a small notched bud. A fairly large fold extending along the lower edge of the left mandible was formed by a hypertrophic fold of mucous membrane covering the left duct of Steno, a hypertrophic sublingual ridge (fig. 1); it simulated part of the tongue. The fold was capable of certain motions. The tonsils were very large, and were divided into an upper and a lower lobe. On crying and, apparently, on swallowing, the tonsils

approximated and practically closed the posterior part of the floor of the mouth. The epiglottis was not flat, as usual, but folded.

The speech was not very clear, but one could understand the patient quite well; she talked much and seemed to have very little difficulty in articulating the words. The child had some difficulty in the swallowing of solid food, and frequently assisted in this act by pushing the food toward the pharynx with the finger; the food then entered the esophagus without any trouble. The anomaly of the epiglottis did not interfere with the function. There was a moderate continuous dripping of saliva, which was aggravated during colds.

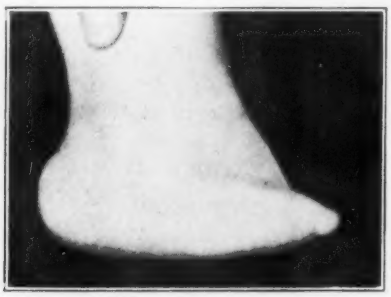


Fig. 4.—Photograph of patient's right foot.

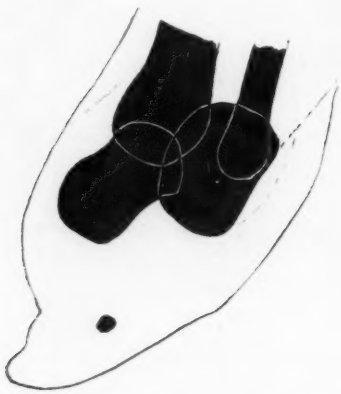


Fig. 5.—Graphic representation of roentgenogram of patient's right foot.

SUMMARY AND COMMENT

In the case reported, there was almost complete absence of the tongue; the notched bud in front apparently represented a rudiment of the lateral tongue swellings. There was no evidence of the part normally formed from the tuberculum impar or of the radix linguae. The nondevelopment of the anterior part of the tongue and the underdevelopment of the mandible occur together, as both originate from the same visceral arch. In cases of agnathia the tongue—at least the anterior part—is always absent. The lower parts of the tonsils help to form a part

of the posterior floor of the mouth. The absence of the lower incisors and the consecutive narrowing of the floor space make it easier for the left hypertrophic sublingual ridge to form part of the floor of the mouth and to aid in the act of mastication, especially as this ridge seems to contain muscle fibers, which make some voluntary motions possible. Teratologically, one has to assume that in the case reported the damage must have occurred at a very early age in order to produce anomalies in so many and in such widely separated organs.

COARCTATION OF THE AORTA (ADULT TYPE WITH HYPERTENSION)

REPORT OF A CASE WITH DIAGNOSTIC ROENTGENOGRAMS

MAY G. WILSON, M.D.
NEW YORK

Coarctation of the aorta or stenosis of the aortic isthmus (adult type) is rarely recognized clinically during childhood. The recent description of diagnostic roentgenologic criteria by Railsback and Dock [1] and Fray [2] should facilitate earlier diagnosis. The comprehensive review of the embryology, pathology and pathologic physiology of coarctation of the aorta by Hamilton and Abbott,[3] Abbott,[4] King [5] and Blumgart, Lawrence and Ernstene [6] makes recapitulation unnecessary.

REPORT OF A CASE

History.—A colored girl, aged 20, had been under observation at the Heart Clinic of the New York Nursery and Child's Hospital since the age of 9 years. She was born in the West Indies, and was the youngest of three children. Her two sisters and the mother were alive and well. The father had died of an unknown cause. The patient was born at full term and developed normally, being free from the usual diseases of childhood. With the exception of pneumonia at the age of 8½ years, from which she made an uneventful recovery, she had been remarkably well. During this illness a systolic murmur was noted, and she was referred to the Heart Clinic for this condition.

From the Department of Pediatrics, Cornell University Medical College and the New York Nursery and Child's Hospital.

1. Railsback, O. C., and Dock, W.: Erosion of the Ribs Due to Stenosis of the Isthmus (Coarctation of the Aorta), Radiology **12**:58, 1929.

2. Fray, W. W.: Roentgenologic Diagnosis of Coarctation of the Aorta, Am. J. Roentgenol. **24**:349 (Oct.) 1930.

3. Hamilton, W. F., and Abbott, M. E.: Coarctation of the Aorta of the Adult Type: I. Complete Obliteration of the Descending Arch at the Insertion of the Ductus in a Boy of Fourteen; Bicuspid Aortic Valve; Impending Rupture of the Aorta; Cerebral Death, Am. Heart J. **3**:381 (April) 1928.

4. Abbott, M. E.: Coarctation of the Aorta of Adult Type: II. A Statistical Study and Historical Retrospect of Two Hundred Recorded Cases, with Autopsy of Stenosis or Obliteration of Descending Arch in Subjects Above the Age of Two Years, Am. Heart J. **3**:392 (April) 1928.

5. King, S. T., Jr.: Stenosis of the Isthmus (Coarctation) of the Aorta and Its Diagnosis During Life, Arch. Int. Med. **38**:69 (July) 1926.

6. Blumgart, H. L.; Lawrence, J. S., and Ernstene, A. C.: The Dynamics of the Circulation in Coarctation (Stenosis of the Isthmus) of the Aorta of the Adult Type; Relation to Essential Hypertension, Arch. Int. Med. **47**:806 (May) 1931.

Examination.—On examination at the age of 9 years she was well developed and in good nutrition. There was noticeable pulsation of the vessels of the neck, and a systolic thrill was felt at the base of the heart. The maximal apical impulse was in the fifth space, 10 cm. from the midline. A rough systolic murmur was heard at the base and was transmitted upward. The radial pulse was 80 per minute; it was under slightly increased tension and the sinus rhythm was regular. The systolic blood pressure over the brachial arteries ranged from 180 to 220 mm. of mercury, the diastolic from 110 to 130 mm. The systolic blood pressure taken over the femorals was 120 mm.

Fluoroscopic examination showed an abnormal pulsation and dilatation of the ascending aorta, with noticeable absence of the aortic knob. The cardiac silhouette was definitely enlarged and duck-shaped. An electrocardiogram showed a normal sequence of cardiac activity, normal conduction time and right-sided preponder-

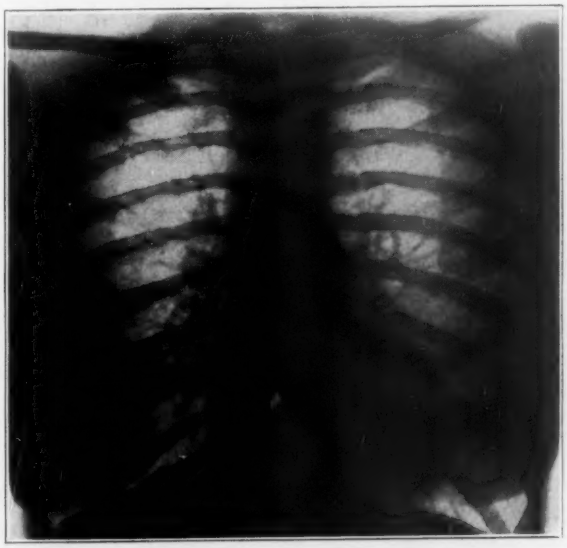


Fig. 1.—Roentgenogram (postero-anterior position) demonstrating: (1) absence of the aortic knob; (2) left ventricular enlargement; (3) dilatation of the ascending aorta, and (4) bilateral scalloping of the lower border of the ribs.

ance. The results of tests of the function of the kidneys were within normal range, and the Wassermann reaction was negative.

Course.—During the eleven years of observation there were no subjective symptoms referable to the circulatory system. The patient was in excellent nutrition, and for the last two years had been employed as a waitress and chambermaid. Subsequent physical examinations confirmed the findings made on first observation. Recent roentgen examination of the chest showed:[7] In the postero-anterior position (fig. 1) there were left ventricular enlargement with absence of the aortic knob and dilatation of the ascending aorta. (These findings were similar to those recorded in roentgenograms taken when the patient was 9 years old.) Of par-

7. The earlier films were inflammable and were recently destroyed. The erosion of the ribs, if present, was not noted at that time.

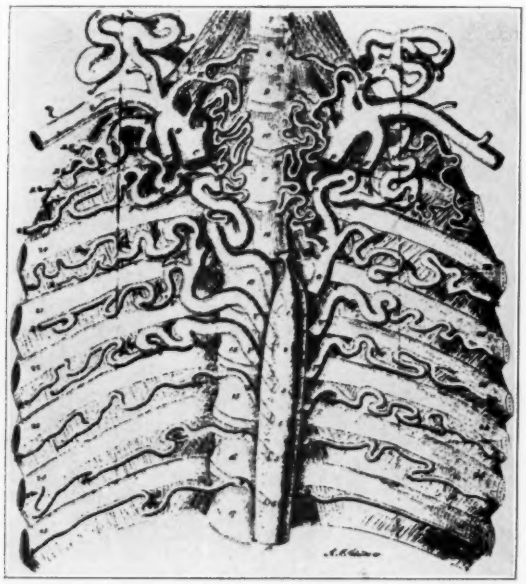


Fig. 2.—Meckel's diagram. (From Meckel, A.: *Arch. f. Anat. u. Physiol.*, 1827, p. 468.)

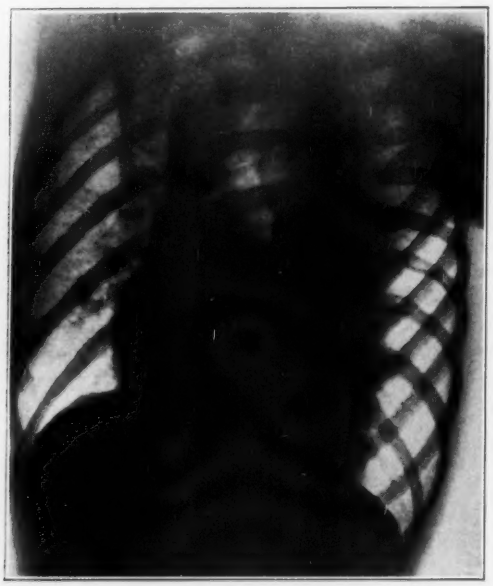


Fig. 3.—Roentgenogram (postero-anterior oblique position) demonstrating: (1) break in the continuity of the aorta and defect in the arch, and (2) dilatation of the descending aorta.

ticular importance was the characteristic bilateral scalloping of the inferior borders of the ribs. Railsback and Dock were the first to show that the erosion of the ribs could be demonstrated roentgenologically. It is of interest that the anatomic demonstration of erosion of the ribs by pulsating dilated intercostal arteries was described by Meckel in 1827 (fig. 2). In the left postero-anterior oblique position (fig. 3), there was evident marked dilatation of the descending aorta, with a break in continuity of the aorta and a defect in the arch. Fluoroscopic examination in these positions confirmed the findings in the roentgenograms.

SUMMARY

The case of a patient observed for eleven years, from the age of 9, demonstrating coarctation of the aorta (adult type) with hypertension, is presented.

The clinical findings were: (1) hypertension of the vessels of the upper extremities, and (2) systolic murmur over the aorta.

Roentgen examination showed: (1) left ventricular hypertrophy; (2) absence of the aortic knob; (3) bilateral scalloping of the lower border of the ribs; (4) dilatation of the ascending and descending aorta, and (5) a break in the continuity of the aorta with a defect in the arch.

Fluoroscopic examination confirmed the findings in the roentgenograms.

161 West Sixty-First Street.

HEREDITARY ECTODERMAL DYSPLASIA, ANHIDROTIC TYPE

REPORT OF A CASE WITH OBSERVATIONS AT NECROPSY

MENDEL ZELIGS, M.D.
CINCINNATI

I am reporting this case because of its extreme rarity. Although the first case was reported over eighty years before this writing, only twelve similar cases are found in the literature, and only one with observations at necropsy.

REPORT OF CASE

W. W., a male infant, aged 10 months, was admitted to the Jewish Hospital on July 22, 1930. His mother stated that since birth, on Sept. 8, 1929, he had been having fever at irregular intervals, but only during hot weather. He had to be sponged frequently, and during very hot weather he had to be kept in a continuous bath. He was never known to have sweated, no matter how hot the weather was. For the past ten days he had had vomiting and diarrhea, from four to fifteen watery stools daily, these occasionally showing small amounts of blood.

The past history, otherwise, was essentially unimportant except that he had been treated by roentgen rays for an enlarged thymus. The family history was unimportant, except that the first and only other pregnancy of the mother had ended in a stillborn child at six months. The parents knew of no instance in their families of a condition similar to that of the patient.

Physical examination showed a long, thin, very blond boy, 10 months of age, who appeared much older. He was restless and irritable. The temperature was 99.8 F. The head was large, being 19 inches (48.2 cm.) in circumference; prominent veins were present. The upper central incisors, the only teeth present, were peg-shaped and widely spaced. The skin was pale and dry. There was an absence of sweat, even in the axillae, although the external temperature was that of hot summer. The hair on the scalp and body was rather sparse, and of very fine texture. The nails were normal. Examination otherwise gave essentially negative results.

Laboratory Data.—Roentgenograms of the heart, lungs, long bones and bones of the skull were normal. The urine was normal except for an occasional trace of albumin. The red blood cells were 5,100,000 per cubic millimeter; the white blood cells varied between 14,000 and 23,000. The polymorphonuclears varied from 31 to 60 per cent and the hemoglobin from 55 to 60 per cent. Intradermal tuberculin

---

From the B. K. Rachford Department of Pediatrics, College of Medicine, University of Cincinnati, and the Pediatric Service of the Jewish Hospital.

Read at the Sixteenth Annual Meeting of the Central States Pediatric Society, Cincinnati, Oct. 17, 1931.

tests and blood cultures gave negative results. The Wassermann tests on the child's and mother's blood were negative.

Course in Hospital.—The temperature was usually normal except for sudden rises, during very hot days, of from 1 to 3 degrees which lasted several hours. On one occasion the temperature rose from 99 to 109 F. in six hours. An ice pack brought it down to 96 F. within an hour. Four hours later it rose to 103 F., and the next day was normal, where it remained, except for occasional rises to 102 F. At no time did the child sweat, even after being given hot milk and wrapped in blankets. The gastro-enteritis continued during his hospitalization. It was not of the type to account for the irregular fever. He grew progressively worse, and in

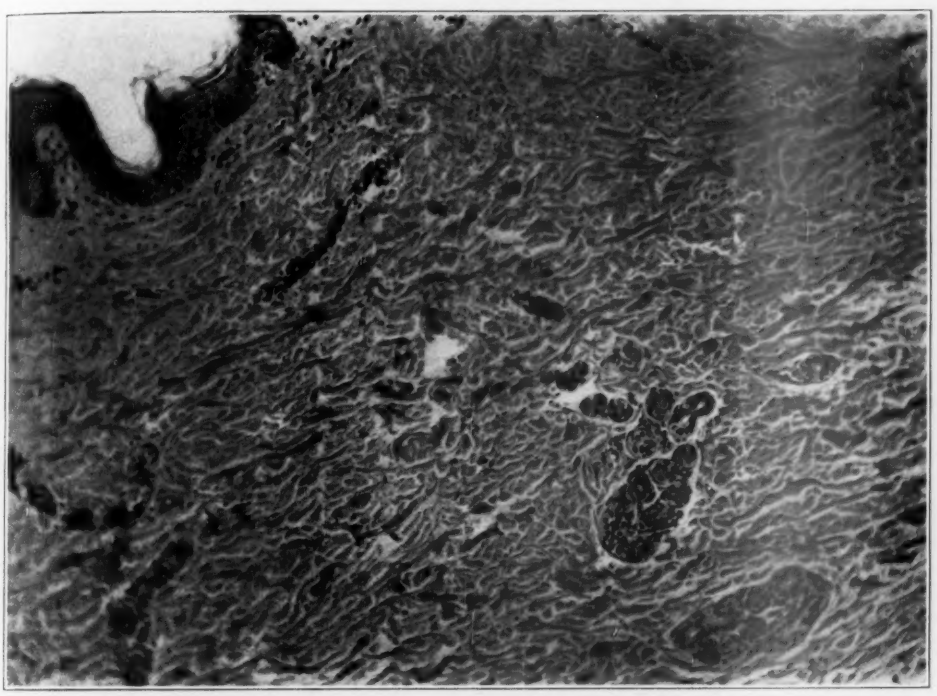


Fig. 1.—Section of skin from abdomen of normal 10 months old boy, showing sweat glands.

spite of transfusions and parenteral injections of fluids, his weight dropped from 18 to 15 pounds (8.1 to 6.8 Kg.); he died a month after admission to the hospital.

Autopsy.—Postmortem examination by Dr. M. Herzberg showed marked congestion of the lower ileum and colon, but otherwise nothing of importance. Microscopic examination showed congestion of the spleen, cloudy swelling of the liver and kidneys, edema and round cell infiltration of the intestines. Sections of skin taken from the abdominal incision were made serially, and although carefully examined failed to show any sweat or sebaceous glands, but the hair follicles were well developed and present in considerable number. Skin from other parts of the body was not examined. Sections of skin from a child of the same age, taken from a similar location by Dr. Pearl Zeek, showed numerous sweat and sebaceous glands.

COMMENT

Hereditary ectodermal dysplasia of the anhidrotic type was first described by Thurman [1] in England in 1848. Weech,[2] who proposed this name for the condition, reported the eleventh case and gave an

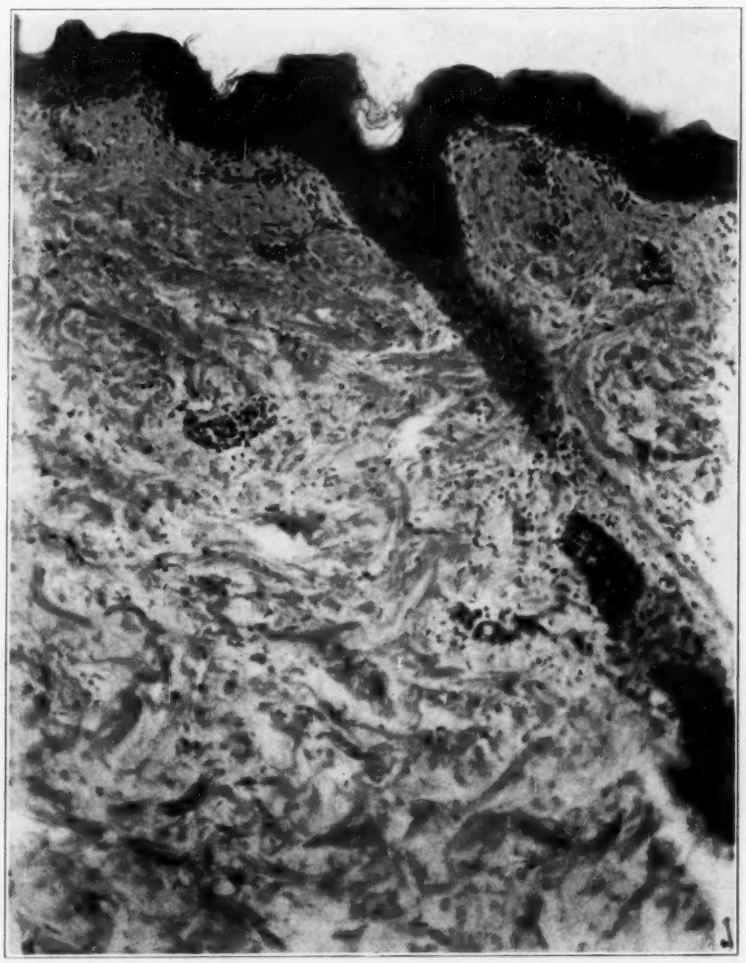


Fig. 2.—Section of skin from patient's abdomen showing hair follicle, but no sweat or sebaceous glands.

elaborate discussion and review of the literature. The twelfth case was reported by Kerley.[3] The characteristic observations are a com-

1. Thurman, quoted by Weech (footnote 2).

2. Weech, A. A.: Hereditary Ectodermal Dysplasia (Congenital Ectodermal Defect), Am. J. Dis. Child. **37**:766 (April) 1929.

3. Kerley, C. G.: Hereditary Ectodermal Dysplasia (Weech), Arch. Pediat. **47**:639 (Oct.) 1930.

bination of congenital absence of the sweat glands and absence of the pilosebaceous apparatus over most of the body, with resulting intolerance for heat. There are marked dental aplasia, a depressed nasal bridge, atrophic rhinitis, prominent supra-orbital ridges and thick, protruding lips. The skin is very white, thin, dry, smooth and soft, and shows the superficial veins plainly. This case differs from the others of this type reported in that, although there is an absence of sweat and sebaceous glands, the hair follicles are normal in appearance and fairly numerous. The only other characteristic observation was the absence of teeth with the exception of the two peg-shaped upper central incisors. The bridge of the nose was normal, but there was a mild rhinitis. The supra-orbital ridges and the lips were not abnormal. As the child was only 10 months old, it is quite possible that atrophic rhinitis with resulting depression of the nasal bridge might have developed later. Unfortunately, only skin from the abdomen was examined microscopically, but the entire block was sectioned serially and carefully studied, and no sweat or sebaceous glands were found.

670 Rockdale Avenue.

HERPES ZOSTER IN THE NEW-BORN

BARNET E. BONAR, M.D.
AND
CLIFFORD J. PEARSALL, M.D.
SALT LAKE CITY

Herpes zoster, uncommon in childhood, is especially so in the new-born period of life. The pediatric texts are singularly vague on the subject, and in many there is no mention of it at all. From the rather scanty information at hand, herpes zoster in infancy most often involves the chest, with frequency of distribution over the abdomen, extremities, face and neck in the order given. The lesions are less painful and tend to heal more rapidly than in the adult, usually healing in ten days if the vesicles are unruptured. For many years herpes zoster has been thought to have some association with varicella, and at present a definite relationship between these two diseases seems fairly well established.

Comby,[1] who has contributed considerable information about herpes zoster in childhood, has seen only eighty-four cases in patients between the ages of 8 months and 15 years, nine of whom were between the ages of 8 months and 2 years. The distribution of the lesions was chiefly on the chest, and no instance of involvement of the arm and hand was recorded. The fact that in eighteen of the twenty-five patients tested the reaction to tuberculin was positive suggests tuberculosis as a predisposing factor. None of these cases showed any apparent connection with varicella.

A few other cases of herpes zoster in infancy have been reported. Thus, Lomer [2] mentioned that Bohn observed two cases in 5 and 7 month old infants, but we have been unable to find the later's article. Pernet [3] described a case involving the lower part of the flexor surfaces of the left arm and forearm in an 18 month old boy. A number of large bullae involving mainly the palmar aspect of the left hand and fingers were also present. This author stated that in his experience

---

From the New-Born Department of the Holy Cross Hospital.

1. Comby, J.: Herpes Zoster in Children, Bull. et mém. Soc. méd. d. hôp. de Paris **46**:992 (June 30) 1922.

2. Bohn, quoted by Lomer: Herpes Zoster bei einem 4 tage alten Kind, Zentralbl. f. Gynäk. **13**:352, 1889.

3. Pernet, G.: Herpes Zoster in the Arm and Hand in an Infant, Brit. J. Child. Dis. **15**:30 (Jan.-March) 1918.

such localization of the lesions was exceedingly rare. McCaw [4] described herpes zoster in a girl of 14 months with lesions distributed over the sole of the left foot between the first and second toes, the posterior aspect of the middle third of the thigh and the outer surface of the labium majoris. The first, second and third sacral nerves were involved. In a personal communication from this author, we were informed that a second attack occurred six months later, with identical distribution of the lesions but a more profuse reaction than in the original attack. He also mentioned two cases reported by Boix.[5] One, in a 2 month old infant, is of particular interest. In the last two weeks of pregnancy, herpes zoster involving the seventh, eighth and ninth intercostal spaces developed in the mother, and cleared up a few days after delivery of the child. Herpes zoster involving the first two intercostal spaces, with a few grouped vesicles in the cervicobrachial region, developed in the infant at 2 months of age. These lesions disappeared after ten days. Frühwald [6] described a case of herpes zoster in a 13 month old boy, the lesions occurring on the right lower quadrant of the abdomen and on the right thigh. This infant had received 0.15 Gm. of neoarsphenamine in the course of five weeks. Knox [7] reported the occurrence of an exceedingly rare form of ophthalmic zoster in a girl of 15 months, and Glaubersohn and Vilfand [8] a case of scapulobrachial zoster in an infant of 25 weeks.

Careful search of the literature has revealed only two instances of herpes zoster in the new-born period, in one of which the diagnosis was made by the presence of scars. Von Reuss [9] mentioned a case reported by Lever in a 4 day old infant, but on carefully checking the references we found that apparently through a typographic error the name Lever should rightly be Lomer.[2] This is the case also referred to by both McCaw [4] and Boix.[5] Lomer was unable to find mention in the literature of herpes zoster at such an early age, and our search leads us to the

4. McCaw, I. H.: Herpes Zoster at Fourteen Months, Brit. M. J. **1**:99 (June 15) 1927.

5. Boix, E.: Nature et pathogénie du zona, Ann. de Fac. de med. de Montivideo **2**:401 (Aug.-Sept.) 1917.

6. Frühwald, R.: Herpes Zoster After Arsphenamine Treatment of Small Child, Dermat Wchnschr. **79**:1579 (Dec. 6) 1924.

7. Knox, R. A.: Herpes Zoster Ophthalmicus in an Infant, Atlantic M. J. **31**:750 (July) 1928.

8. Glaubersohn, S. A., and Vilfand, R. A.: Changes in the Spinal Fluid in Zoster in an Infant Aged Twenty-Five Weeks, Dermat. Wchnschr. **82**:1299 (Sept.) 1920.

9. von Reuss, A.: Diseases of the Newborn, English translation, New York, William Wood & Company, 1921, p. 398.

conclusion that his case was the first to be recorded. Kalb [10] described a case in a new-born child in which there were multiple grouped scars symmetrically arranged in the area of the first and second branches of both trigeminal nerves, which he considered to be the remains of a bilateral intra-uterine herpes. Kocks [11] in the same journal supported the view of Kalb.

We have had the fortune to observe what appears to be the third case of herpes zoster in a new-born infant, if the case of Kalb is to be considered authentic. The case record follows.

REPORT OF A CASE

History.—A girl, M. M., white, was born on March 10, 1931. She was the second child. Dr. H. P. Kirtley, the accoucheur, stated that the labor lasted seven hours and forty minutes. The vertex presented, and the position was right occipitoposterior, which rotated spontaneously. Little difficulty was encountered in delivering the shoulders. The birth weight was 7 pounds and 5 ounces (3,370 Gm.). The father's health was good, as was that of the 3 year old brother. The mother had not felt well during pregnancy. The infant was normal at birth, and lost only 5 ounces (150 Gm.) in the first three days, after which she started to gain. On the second and third day the temperature rose to 99.8 F., but subsided promptly when the breast milk appeared.

On the afternoon of the fourth day, the nurse reported a blister on the dorsum of the right hand, which looked to her like a burn, but which she could not account for in any way as no external heat had been applied.

Examination.—Fifth Day: The infant appeared normal save for a mild icterus. Physical examination revealed no abnormalities except the skin lesion located on the extensor surface of the right hand over the first metacarpal bone. The nurse reported that the lesion had been a blister, but at the time of examination it was a shallow linear ulcer with a regular margin and a clean, moist base. The ulcer was 1 cm. long, 0.3 cm. wide and 0.3 cm. deep, its long diameter parallel to the metacarpal. No diagnosis was made at this time.

Sixth Day: The original ulcer had become crusted. Extending up the hand and wrist were closely packed groups of vesicles situated on an edematous, reddened base. The vesicular fluid was yellow. A diagnosis of herpes zoster was made, which was corroborated by further observation.

Seventh Day: The vesicles had extended up the extensor surface of the forearm onto the arm, and at the point where the radial nerve passes around the humerus the lesions were similarly directed. The infant seemed to be suffering no pain. The initial loss in weight was regained by the fifth day, and the baby continued to gain. The temperature became elevated to 100.6 F. on the twelfth day. Between the seventh and the tenth day new groups of erythematovesicular lesions continued to appear, the older lesions becoming dry and crusted.

Tenth Day: An examination of the blood on March 19 revealed: hemoglobin, 88 per cent; erythrocytes, 5,101,000, and leukocytes, 11,900. The differential count

10. Kalb, O.: Ueber angeborene multiple symmetrisch gruppiert Narbenbildungen im Gesicht, Zentralbl. f. Gynäk. **33**:929, 1909.

11. Kocks: Doppelseitigkeit des Herpes Zoster faciei und der Fall Kalb, Zentralbl. f. Gynäk. **33**:1232, 1909.

showed: polymorphonuclear neutrophils, 54 per cent; small lymphocytes, 23 per cent; large lymphocytes, 2 per cent, large mononuclears, 2 per cent, and basophils, 1 per cent. Up to this time the lesions had been painted with an antiseptic lotion, but because of continued extension of the disease 1 minim (0.062 cc.) of a standard obstetric solution of pituitary was injected intramuscularly. The infant became distressed within one minute; she defecated, and the skin became moderately cyanotic. This reaction lasted about fifteen minutes.

The lesions appeared drier the next day, and no new lesions had appeared, but because of the reactions to solution of pituitary by hypodermic administration, a pledglet of cotton soaked with 0.5 cc. of the preparation was inserted into the nostril for two minutes. The infant again appeared distressed and had an evacuation of the bowels, but the reaction was much less severe than on the previous day.

Subsequent Course.—Intranasal administrations of solution of pituitary were continued daily for eight days. Each time the infant reacted as has been described. The lesions gradually dried up, and on the nineteenth day were practically healed, leaving red scars on the hand and wrist. The general condition of the child remained good, and she has continued to thrive.

A negative Pirquet test was obtained during the sixth week. On April 30 (the fiftieth day), the results of examination of the blood were: hemoglobin, 60 per cent; erythrocytes, 4,110,000, and leukocytes, 10,300. The differential count showed: polymorphonuclear neutrophils, 27 per cent; small lymphocytes, 32 per cent; large lymphocytes, 40 per cent, and large mononuclears, 1 per cent. Communication with the mother revealed the fact that at the age of 3 months, nine weeks after the first attack had subsided, blister-like lesions again appeared in the region of the scar on the hand and wrist. These vesicles were filled with clear fluid. One vesicle also appeared on the right side of the flexor surface of the ring finger. These lesions lasted only four or five days. A similar eruption appeared on the right forearm at the fourth month, the lesions disappearing in a few days.

Mother's History.—It has been stated that the mother's condition toward the termination of pregnancy was not normal, although nothing definite could be found at examination. On the twelfth day, post partum, injections were made into bothersome varicose veins of the left leg. Three days later, thrombophlebitis of the left femoral vein appeared. Five days later, the temperature became elevated again; rapid, grunting respirations appeared, and on examination a small area of consolidation could be demonstrated in the left lung. One week later, fluid developed in the left pleural cavity, and 400 cc. of a clear straw-colored fluid was removed. This fluid was injected into the peritoneal cavity of a guinea-pig. At six weeks the animal showed no evidence of tuberculosis. The mother showed improvement following thoracentesis, and six months post partum her health was said to be excellent.

COMMENT

The etiology of this case is not clear. The mother's health before delivery was poor, and the development of pleurisy with effusion afterward suggests tuberculosis. In this event the herpetic lesions might be attributed to the toxins of tuberculosis, as such an etiology is not unknown.

However, inoculations with fluid obtained from thoracentesis into a guinea-pig proved innocuous to that animal, and at the time of writing, six months after delivery, the mother's condition is much improved.

The infant reacted negatively to the Pirquet test. The facts that the respiratory symptoms in the mother appeared after injections had been made into varicose veins of the legs, and that they were followed by the development of pleural effusion are highly suggestive that the pulmonary findings were of an embolic nature.

Trauma to branches of the brachial plexus from traction on the head during delivery of the shoulders must be considered a factor in the case, since herpes has been known to follow trauma of the posterior roots. Although Dr. Kirtley informed us that little traction on the head was necessary to deliver the shoulders, and he feels that trauma could not be considered a factor, the fact that the lesions recurred in a few months seems to lend strength to the traumatic theory of origin.

Symptomatically, little could be observed. The infant did not appear disturbed by the lesions; there was very little influence on the temperature, and the blood picture was normal for a baby of the patient's age.

Treatment with solution of pituitary hypodermically and intranasally seemed to be of value in shortening the course, but as it is known that lesions clear up rapidly in childhood, the effect of the treatment cannot be definitely established.

Recurrence of the lesions at the third and fourth month is uncommon, yet it has been known to occur (McCaw [4]).

CONCLUSIONS

Herpes zoster is rare in childhood, especially in the new-born period. A third case of herpes zoster in a 4 day old infant is reported. The etiology of this case is obscure, but certain factors lend support to its being of traumatic origin. The lesions were apparently painless and seemed to be influenced favorably by solution of pituitary. Intranasal administrations of this solution caused an immediate but less violent reaction than intramuscular injection.

9 Exchange Place.

Progress in Pediatrics

CAPILLARY MICROSCOPY IN CHILDREN

SIDNEY D. LEADER, M.D.
NEW YORK

Although capillary microscopy was originally described in 1912 by Lombard, little work has been done in this country on the morphology of capillaries in children. Abroad, Müller, Jaensch, Hoepfner and others have made some striking contributions; but for the most part, the physicians in this country are unaware of their work and of capillary microscopy in general. For this reason, I shall briefly review the significant literature and also append a few of my own observations.

The interpretation of capillary visualization depends a good deal on the point of view of the individual observer. Though capillary structure is quite definite, unless great care is exercised, deformities and abnormalities may be read into a normal picture if the observer is of an imaginative disposition. Even the interpretation of photomicrographs of capillaries may vary with the individual. In my own work I have considered all capillaries normal unless an undisputed pathologic structure was found.

For a better understanding of the capillary picture, the anatomy and histology of the vessels and of their adjacent tissues are presented [1] (fig. 1).

The number and size of the vessels running to the skin vary in different situations, the number being greater in those regions that often experience external pressure, such as the palms and soles. All of the branches of these arteries anastomose freely with each other and with adjacent vessels, and thus form a characteristic cutaneous arterial network in the deepest layer of the cutis where it joins the fat. From this mesh, arched and branching vessels proceed outward and, anastomosing, form a subpapillary arterial network near the junction of the middle and outer thirds of the cutis. Numerous small branches arise from this network and run as terminal arterioles to the superficial layers of the skin. These turn and course for a short distance parallel to the skin in the direction of the papillary ridges beneath which they run. They send

From the Department of Pediatrics of the Mount Sinai Hospital, Service of Dr. Béla Schick.

1. Spalteholz, W.: Arch. f. Anat. u. Physiol., 1893.

their twigs to the arterial limbs of the capillary loops lying in the papillae. The venous blood returning from the papillae passes through several networks, forming the subpapillary venous plexuses. One is slightly above the arterial plexus; another lies immediately beneath the arterial plexus; a third and fourth are at the level of the junction between the cutis and the subcutis. Normally, there is present only one capillary loop to each papilla of the cutis.

The histologic structure of the capillaries has long been a subject of great dispute. Until recently, it was believed that this structure consisted of only a single layer, the endothelial lining. Recently, however, some investigators have expressed the belief that certain cells first described by Rouget [2] in 1873 in amphibia are also present in the capillary lining of human beings. In 1923, in a thorough histologic study,

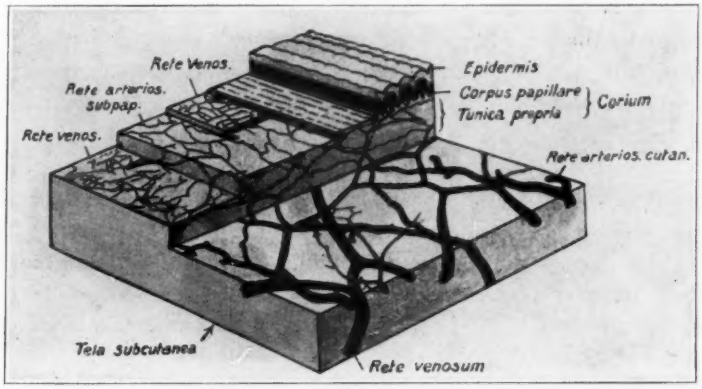


Fig. 1.—Reconstruction of blood vessels of the skin (Spalteholz).

Vimtrup [3] proved to the satisfaction of Krogh and others [4] that these cells could be observed in the capillaries of human beings. The cells are spindle-shaped smooth muscle cells having the power of contracting and expanding and giving the capillaries their tonus. Roy and Brown,[5] Hooker [6] and Cotton, Slade and Lewis [7] have conclusively shown that capillaries are not merely passively distended by arterial pressure, but possess a tone of their own and may show contractions and relaxations independent of the corresponding reactions in the arteries.

---

2. Rouget, C.: Arch. d. Physiol. **5**:603, 1873.

3. Vimtrup, B.: Ztschr. f. d. ges. Anat. **65**:150, 1922; ibid. **68**:469, 1923.

4. Krogh, A.: Anatomy and Physiology of Capillaries, New Haven, Conn., Yale University Press, 1929.

5. Roy, C. S., and Brown, I. G.: J. Physiol. **2**:323, 1879.

6. Hooker, D. R.: Am. J. Physiol. **54**:30, 1920.

7. Cotton, T. F.; Slade, J. S., and Lewis, T.: Heart **6**:227, 1917.

This phenomenon has led Lewis and other investigators to search for the exciting factors. That the sympathetic nervous system controls the smooth musculature of the capillaries as it does that of other blood vessels has been shown through a series of experiments by Krogh and others.[4] Nevertheless, possibly because the nerves are so minute, histologic studies have never revealed an innervation of the capillaries themselves.

Lewis [8] has demonstrated that there is another factor in the regulation of capillary expansion and contractility. The classic experiments analyzing the reaction of the skin to stimuli tend to prove that capillary dilatation is not merely passive but is the result of the excretion by adjacent cells of a substance resembling histamine. This substance is present normally in the tissues surrounding the capillaries, and is called forth only in response to an irritating stimulus.

Internal secretions, such as epinephrine [9] and pituitary,[4] acting on the smooth muscle or its innervating mechanism are also responsible for the physiologic responses of the capillaries, causing contraction.

A thorough understanding of capillary dynamics must include: (1) a study of the reaction of these vessels to stimuli—mechanical, thermal, electrical and chemical, (2) an appraisal of capillary blood pressure and (3) a microscopic visualization of their appearance together with observations on the capillary blood flow.

For the present I have limited myself to capillary morphology and a study of the blood flow in childhood. With few exceptions, my observations were made on the capillaries of the nail bed. As the capillary layers of the skin and the epidermis pass over into the subungual space, the capillary loops are horizontally placed and easy to observe. It is for this reason that the nail bed is used as the region for study. In general, these capillaries are constant in number, and under normal circumstances they remain patent all the time. In this they differ from the vessels in other parts of the body, where, as Krogh has shown, not all of the capillaries are filled, but on exertion, irritation and stimulation, more vessels are opened. The blood flow in the vessels of the nail bed is somewhat slower than that in the other capillaries.

TECHNIC

The apparatus for the visualization of the vessels is a very simple one. In 1912, Lombard,[10] in studying capillary blood pressure, found that the superficial vessels are rendered clearly visible when the skin is illuminated and a highly refractile oil

8. Lewis, Sir T.: Blood Vessels of the Human Skin and Their Responses, London, Shaw & Sons, Ltd., 1927.

9. Dale, H. H., and Richards, A. N.: J. Physiol. **52**:110, 1918.

10. Lombard, W. P.: Am. J. Physiol. **29**:335, 1911.

is placed on it. This method has undergone development in the hands of Müller [11] and Weiss,[12] and this modification is generally used at the present time. My apparatus consists of a high-powered lamp with central illumination, the light being concentrated by a convex lens. The light is filtered by a blue medium which eliminates both the heat rays and the ultraviolet rays. This increases the clarity with which the vessels are seen, though its primary purpose is to prevent the reaction of the cutaneous vessels to heat. (A convex flask filled with water colored with methylene blue is an excellent substitute for a converging colored lens.) The ray of light is focused on the stand of a low-power microscope. The finger to be observed is placed under the microscope, the region just proximal to the root of the nail being selected for observation. In treating the skin beforehand, the surface may be cleaned and dehydrated with alcohol to remove scales, dirt, fat globules and perspiration. The skin should not be rubbed, since any irritation will alter the

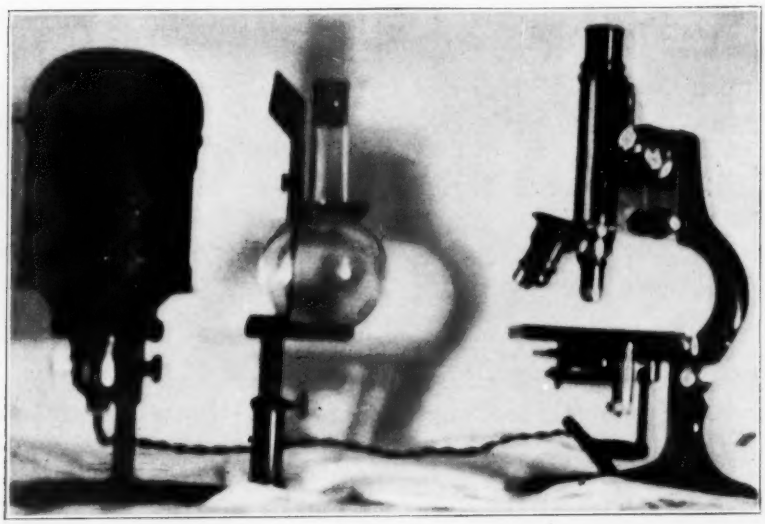


Fig. 2.—Instrument for visualization of the capillaries of the nail bed.

natural circulation and structure of the vessels. After cleansing the skin, I allow several minutes to elapse to let the vessels resume their original appearance, if perchance a slight hyperemia has been set up. A drop of cedar oil is then placed on the skin to be observed. The oil aids in cutting out abnormal light reflexes.

With this apparatus a magnification of one hundred diameters is obtained, and observation can be made through the superficial layers of the skin down to the middle of the cutis.

It must be remembered that in microscopic examination of the capillaries, not only the capillary wall per se, but the constant stream of blood flowing through the vessel are observed. For this reason many terms

11. Müller, O.: Die Kapillären der menschlichen Körperoberfläsche in Gesunden und Kranken, Stuttgart, Ferdinand Enke, 1922.

12. Weiss, E.: Deutches Arch. f. klin. Med. **119**:1, 1916.

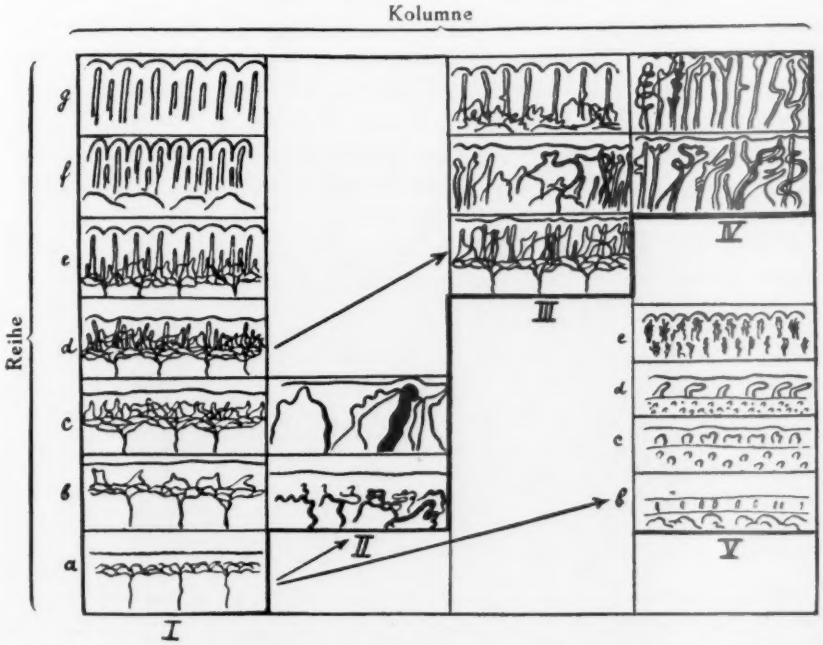


Fig. 3.—Development of skin capillaries, normal and pathologic (Jaensch and Hoepfner). Column *I* shows the following normal development: *a*, primitive network with flat-shaped corium observed shortly after birth; *b* and *c*, saddle-shaped and turret-shaped loops sprouting at from 5 to 6 weeks of age; *d*, *e* and *f*, formation of hairpin loops, differentiation of venous and arterial components, development of scalloped corium and disappearance of subpapillary plexus; *g*, mature form reached at from 6 months to 6 years of age. Columns *II*, *III*, *IV* and *V* show abnormal forms derived from the various stages of development.

Fig. 4.—Development of capillaries of the skin (Müller). At the age of 2 weeks, a definite primitive subpapillary plexus is found, and no true capillary loops are seen.

referable to the capillary structure are used loosely. When I refer to spasm or dilatation of the capillary wall, I am merely assuming the presence of such a reaction in view of the fact that the corpuscular filling of the vessel gives that impression.

Normally, the capillary picture is a constant one and does not change from day to day, once the mature stage is attained. However, the

Fig. 5.—Development of capillaries of the skin (Müller). At the age of 1 month, gradual disappearance of the subpapillary plexus and beginning sprouting of the capillary loops from the foundation network are noted.

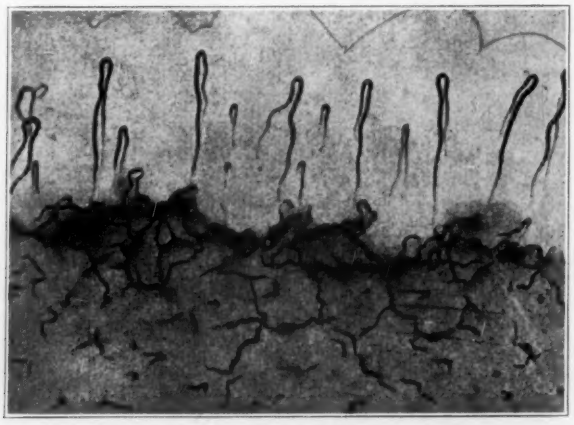


Fig. 6.—Development of capillaries of the skin (Müller). At the age of 3 months, the subpapillary plexus is almost gone. The capillary loops are fairly well developed; they are long, thin and evenly distributed.

development of the capillaries from birth to maturity is interesting (figs. 3, 4, 5 and 6).

At birth, there are no capillary loops. The structure of the vessel consists of a primitive network supplied by the arterioles and venules of the deeper layers. The corium is flat.

At the age of 4 or 5 weeks, widespread saddle-shaped forms sprout from the primitive plexus. Gradually, they develop into the slender hairpinlike capillary forms which do not appear in large numbers until about the fifth month. At the same time, the horizontal network of fine blood vessels decreases in size and complexity, and the corium becomes wavy. When definite loops appear, the corium assumes the scalloped appearance. At from 6 months to 1 year of age, the mature capillary pattern is formed. From then on, the capillary morphology remains constant, though the loops may lengthen and become narrower and more tortuous with advancing age.

The normal capillary consists of a hairpin-like loop of regular contour, not tortuous, exhibiting a constant flow of blood. There is one capillary to each papillary tuft. The size of the vessel may vary, depend-

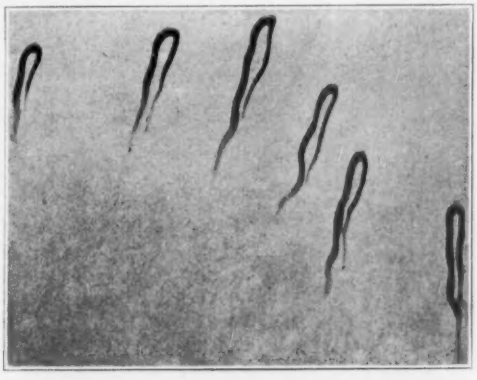


Fig. 7.—Normal capillary picture at nail bed (Müller).

ing on the individual. Both the very long loop and the short loop are normal. The venous limb is slightly larger than the arterial limb.[13] There is no evidence of a subpapillary plexus (figs. 7 and 8).

No two sets of capillaries have an identical pattern. As in the case of fingerprints, no two are exactly alike, though they can be classified into various shapes and patterns. In children, any tortuosity is abnormal.

The blood flow is rapid and the blood column is continuous. Occasionally, a vessel may be seen in which the flow is sluggish at times, but it quickens in a few moments. No pulsatile flow normally occurs in the capillaries. When the flow becomes slow, the column no longer has its normal continuous appearance, but is broken into segments separated by colorless areas. This has been called "granular streaming." It represents some disturbance of the capillary circulation.

13. Crawford, J. H.: J. Clin. Investigation **2**:351, 1926.

No single capillary form is pathognomonic of a given disease. Certain factors influence the capillary vessels and their flow of blood. In disease, because of these influences, the capillary picture is changed.

As has been shown by studies of families, capillary form is not inherited, nor do children of similar blood groups show similar capillary pictures. The constitutional type of the individual affects the capillary picture only when there are vasoneurotic stigmas.

The factor of most importance controlling the morphology of the capillaries is that which causes a faulty development of these vessels.

When the general development of a person is arrested, a pathologic development of the vessels results. Instead of the capillaries developing in the manner outlined previously, they tend to retain some of the

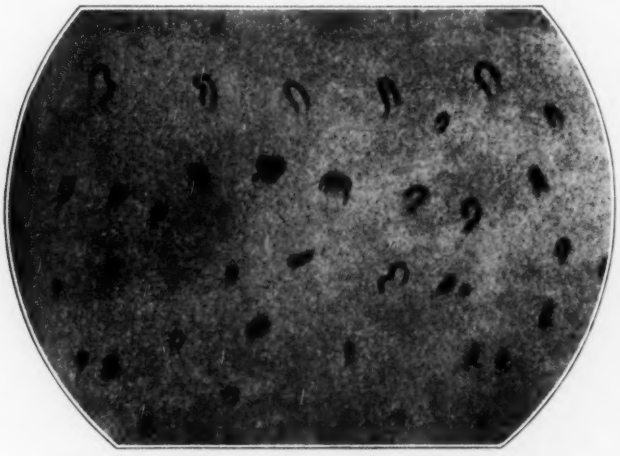


Fig. 8.—Normal capillary picture at nail bed (Boas).

characteristics of their primitive shapes and to assume bizarre forms. Hoepfner [14] has elaborated a pathologic developmental scheme intimately related to the various stages of normal development. According to him, there may be a very early arrested development, giving rise to a capillary pattern that has never lost its primordial characteristic (the subpapillary network), though because of corrective tendencies the capillaries may approximate normal forms.

Then there may be an abnormal progress in the intermediate stages ot development. The relatively large calibered, broad, saddle-shaped loops with undifferentiated venous and arteriole branches and the flat corium are still retained though somewhat modified.

---

14. Hoepner and Jaensch, W.: Die Haut Kapillärmikroscopie, Halle, Carl Marhold, 1929.

There may also be deviations from the ideal normal form which do not show the characteristics of the aforementioned groups, but manifest their deviations in the size of the capillaries or irregularities of arrangement or in the appearance of cork-screw types.

Finally, there may be a deviation from the primitive or intermediate forms, which is called the hypoplastic type, consisting of thin, small-looped vessels having the same characteristics as the primordial types, i. e., the flat corium, the undifferentiated network and wide loops.

Jaensch and Hoepfner [14] found a correlation between these pathologically developed capillaries and a general defect in the mental development of the so-called psychophysical personality.

Wittneben,[15] Kahle [16] and others have confirmed this observation, though Delbruch [17] stated that he found pathologic types in normal and superior children. Powdermaker,[18] in studying the mental defectives at Letchworth Village, came to the following conclusions: In constitutional idiots and low grade imbeciles, in whom there is a high proportion of physical abnormality, there is a marked tendency to retarded or abnormal physical development of the capillaries; this is less striking in patients with normal physical development. In the moron and high imbecile type the primitive forms are fewer. In neurologic disorders of secondary origin, no primitive forms are found.

There are various theories [19] concerning the origin of these pathologic forms.

Doxiades contended that these forms are fetal anomalies, in contradistinction to the views of Hoepfner and Jaensch that they are due to a lack of differentiation of the early developmental stages.

Jaensch feels that the evolution of the capillaries coincides with the myelinization of the nerves and the differentiation of the cerebral cortex. Thus, normally a coordination is established between the skin and the nervous system.

Marinesco stated that the endocrine glands also affect capillary structure. These glands control the development of all tissues derived from the ectoderm and the mesoderm, and therefore the nervous system, the endocrine glands and the skin are intimately correlated. The constitutional development of the abnormal types, the "asthenique," "pycnique" and "dyplastique" types of Kretchmer, influence the capillary structure

---

15. Wittneben, W.: Ztschr. f. Kinderforsch. **22**:4, 1926.

16. Kahle, H. K.: Arch. f. Psychiat. **81**:629, 1927.

17. Delbruch, H.: Arch. f. Psychiat. **81**:606, 1927.

18. Powdermaker, F.: Capillary Forms in Relation to Certain Problems in Development, Arch. Neurol. & Psychiat. **22**:1207 (Dec.) 1929.

19. Marinesco, G., et al.: Bull. Acad. de méd., Paris **103**:596, 1930.

through their vasoneurotic diathesis. Thus, according to Marinesco, all vasoneurotic disturbances have a constitutional basis. Müller, too, is of this opinion.

In mongolian idiocy there is marked evidence of pathologic and retarded development. The primordial subpapillary plexus is present, the capillary loops are irregularly shaped, with the venous and arterial limbs undifferentiated, the corium is flat or slightly wavy, and in some cases grotesque capillary forms appear.

In myxedema, the capillary structure is somewhat similar to that seen in mongolism. Development is retarded, though the capillary forms show less tendency toward the grotesque pathologic state, and develop toward the normal with thyroid treatment. Not all of this improvement can be ascribed to treatment, since the capillaries in untreated cases of myxedema will also develop to some degree toward the normal as the child grows older. In goiter regions the capillaries of the children are normally developed, but they do not reach their mature form until the child is from 3 to 6 years of age, instead of 6 months.[18] In exophthalmic goiter in children, the vessels are large, somewhat tortuous and of excellent tonicity, and they have a continuous stream of blood in contradistinction to the characteristics of the vessels in myxedema.

In hypopituitarism and Fröhlich's syndrome, the capillary morphology resembles that in myxedema. The vessels are those seen in arrested and pathologic development.

Another factor affecting capillary structure is its peculiar predisposition to excitation (vasoneurotic diathesis of Parrisius and Müller). This vasomotor instability is based on a constitutional status and is but rarely purely acquired, though it may become intensified by postnatal stresses.

The capillary pattern in vasomotor instability is fairly typical. It is usually seen in children with mottled skins, cold, clammy extremities and cyanotic finger-tips. The vessels at the nail bed are long, tortuous, somewhat atonic and distended and filled with sluggish blood, though no definite stasis exists. The picture greatly resembles that seen in Raynaud's disease and acrocyanosis.

Raynaud's disease has been thoroughly investigated by Buerger,[20] Brown [21] and others. They noted that during attacks of pallor of the extremities, the capillaries are incompletely filled, many loops are invisible, the flow of blood either ceases or is very slow, and the blood when visible has a cyanotic hue. The transition from pallor to cyanosis is imperceptible. The capillaries slowly dilate and become distended with cyanotic blood. The vessels become large, tortuous and atonic.

---

20. Buerger, L.: Circulatory Disturbances of the Extremities, Philadelphia, W. B. Saunders Company, 1924.

21. Brown, G. E.: J. Clin. Investigation **9**:115, 1930.

In acrocyanosis [22] and scleroderma, the picture is somewhat similar to that seen in the cyanotic state of Raynaud's disease.

Olkon [23] recently described a case of so-called spasmophilic epilepsy in which the vessels were spastic, irregular, dilated, empty and atonic. These vessels were to my mind similar to those seen in other cases of vasomotor instability. Pototsky [24] found the type of capillary seen in vasoneurosis in certain cases of enuresis.

The capillary morphology is frequently altered in cardiac and pulmonary diseases and diseases of the general vascular system. Duken [25] observed a definite capillary pattern in cases of clubbing due to chronic pulmonary disease. The vessels are long and tortuous, dilated and spastic. There is granular streaming, but no definite stasis. The vessels are increased in number. When no clubbing results in these diseases, the capillary pattern remains normal.

Acquired cardiac disease in children offers no characteristic capillary picture. When there is a long-standing hypertension, the result of cardiac or renal disease, the vessels become increased in size and tortuosity.

In congenital heart disease associated with cyanosis the vessels are increased in number, long and tortuous, and are filled with corpuscles moving at a slow rate.

In acute glomerular nephritis, which by some is considered a general capillary disease, the vessels are described as tortuous, thin and spastic, with a segmental flow of blood, and they are somewhat diminished in number.

In nephrosis of long duration, the vessels are increased in number, long, irregular and tortuous, and they sometimes assume bizarre shapes. Occasionally there is an anastomosis of the vessels, and the subpapillary plexus is visible.

Müller [11] found dilatation of the capillaries in diabetes, which he feels is due to a relaxation of the vessel walls with a correspondingly low capillary pressure.

In general, in the acute infections, such as pneumonia and meningitis, and in the fevers, such as typhoid fever, scarlet fever and measles, nothing abnormal is encountered. In serum sickness and other rashes the capillaries are normal. In dyscrasias of the blood no abnormal structure is seen.

---

22. Boas, E.: The Capillaries of the Extremities in Acrocyanosis, J. A. M. A. **79**:1404 (Oct. 21) 1922.

23. Olkon, D. M.: Epilepsy of the Angiospastic Variety in Monozygotic Twins, Arch. Neurol. & Psychiat. **25**:1111 (May) 1930.

24. Pototsky, C.: Enuresis, Am. J. Dis. Child. **40**:46 (July) 1930.

25. Duken, J.: Ergebn. d. inn. Med. u. Kinderh. **34**:457, 1928.

In the main, my own observations have confirmed those previously described. There are, however, a few additional comments which my studies warrant.

The observations made by Powdermaker [18] on children with arrested physical development accompanied by delayed mentality showed the capillaries to be pathologically developed. I examined a group of eighteen children with delayed physical development but of normal or superior intelligence (as evidenced by their school grades and a few gross tests). Their capillaries were normal in all respects.

My observations in mongolian idiocy are interesting. Of the fifteen children examined, eleven showed definite evidence of retarded and pathologic development of the capillaries of the nail bed. This tendency

Fig. 9.—Capillary picture in mongolism. Note the retarded development of the capillaries, the primitive subpapillary plexus, irregularly shaped capillary loops, with no differentiation between the venous and the arterial limbs, occasional grotesque forms, and the wavy corium.

was most marked in those children whose intelligence was lowest and whose physical development deviated furthest from the normal. The four mongoloids with capillaries which approximated normalcy were well above the average patient with mongolism both physically and mentally (fig. 9).

On observing the capillaries of several patients with myxedema who had been under thyroid medication, I was impressed by the rapidity with which the vessels tended to advance to the normal forms, in spite of the fact that the children themselves still remained physically and mentally retarded. I feel that thyroid treatment for myxedema definitely accelerates the tendency of the capillaries toward normal development.

In epilepsy, I have found no typical capillary pattern. In eight of the twelve cases observed, the capillaries were entirely normal. In two, the pattern was that of vasomotor instability (somewhat similar to Olkon's [23] observation). In the other two, the capillaries showed evidence of retarded development—the bizarre shapes, the subpapillary plexus and the irregular corium.

I studied fifteen cases of enuresis in children ranging from 3 to 10 years of age. In none of these cases was I able to find abnormalities such as those described by Pototsky.[24]

Perhaps the most striking of my observations were made in certain cases of bronchiectasis, pulmonary abscess and chronic cardiac disease.

Fig. 10.—Capillary picture in clubbed fingers associated with pulmonary and cardiac disease. The capillaries are long and tortuous, somewhat spastic and dilated. Granular streaming is seen, though there is no stasis. The vessels were normal in number. Change in the vessels antedates gross clubbing.

I examined children with conditions of these types for a long time as a routine, and found that in those cases in which clubbing subsequently developed the definite capillary pattern of advanced clubbing was established in the preclubbing stage. It is thus possible to predict the development of clubbing in this type of case (fig. 10).

Twelve diabetic children were examined, and only two of them showed abnormal capillaries, the vessels being somewhat increased in size, number and tortuosity. Both of these children had had diabetes for several years. In no child did I find dilated capillaries such as Müller described.

In the dyscrasias of the blood, leukemia, the purpuras, hemophilia and the anemias, I found no characteristic picture. I saw a break in the capillary wall with extravasation of corpuscles into the adjacent tissues in only one instance, that of a child with hemophilia.

SUMMARY

1. The anatomy and physiology of the capillaries are briefly discussed.

2. In children the normal capillary picture is constant.

3. The capillary loops are not present at birth, but gradually develop and reach their mature forms at from 6 months to 1 year of age.

4. In disease the capillaries are influenced by (*a*) external stimulation, (*b*) pathologic development, (*c*) vasomotor instability and (*d*) cardiac and pulmonary disease and disease of the general vascular system.

5. In general, the morphology of the capillaries of the skin is not pathognomonic for specific diseases. Certain capillary forms are frequently found in such diseases as nephritis, diabetes, rheumatic fever and arthritis, but these forms are not always present; they may be seen in various other conditions and are occasionally seen in normal persons.

6. Observations in the following diseases of childhood are presented: (*a*) the typical pattern of arrested development in mongolism; (*b*) the capillary morphology in myxedema, with its tendency toward normal development with thyroid therapy, and (*c*) the capillary pattern in bronchiectasis, abscess of the lungs and chronic cardiac disease in which capillary changes precede the appearance of clubbing.

Pediatrics in Art

NECROPSY ON THE NEW-BORN

JOHN RUHRÄH, M.D.
BALTIMORE

Johann van Neck (1636-1714) painted the portrait of Frederick Ruysch (1638-1731) demonstrating the circulation of the placenta and the child, while his son, Hendrik Ruysch, himself later a physician,

Portrait by Johann van Neck.

stands next to him holding a skeleton of an infant. The lace and rich clothing suggest that the lot of the physician in those days brought material rewards.

Ruysch sold his collection of anatomic preparations to Peter the Great for 30,000 gulden. His name is associated with the membrane underlying the choroid, the injection of anatomic preparations, the vessels connecting the placenta and child and other anatomic structures. The photograph is by Hanfstaengl.

Pediatric Biographies

NICOLAS BOURBON
1503-1550 (?)

JOHN RUHRÄH, M.D.
BALTIMORE

Nicolas Bourbon, styled The Elder, was born in Vandeuvre, a village not far from Bar-sur-aube, in the diocese of Langres. His father was evidently a rich man, and Niceron in his "Mémoires pour servir à l'histoire des hommes illustres dans la république des lettres" (1729-1745) stated that he was a *maître d'une forge,* or owner of a factory that was in this village, and not a *forgéron,* or smith, as Pellison stated in his "Histoire de l'académie française." A small point, perhaps, but it shows the easy circumstances in which Nicolas grew up. His mother was named Marie Gallare. He had a tutor Jacques Tousan, and became so proficient in literature and Greek that he was chosen preceptor for Jeanne d'Albret, daughter of Marguerite, queen of Navarre, whose interest in literature is attested by the Heptameron which she bequeathed to posterity. After several years in the employ of Queen Marguerite he retired from the hurly-burly of the court to a small estate in Cande, a little village on the borders of Anjou and Touraine, and there he ended his days.

In 1535, when Bourbon was in England, Hans Holbein did a black and colored crayon portrait of him which is now in Windsor Castle. This the artist later did on wood, and it was used in the 1536 and 1538 edition of Bourbon's poems. It is also reproduced in Knackfus' book on Holbein. In return the poet wrote some introductory verses in praise of Holbein's cuts for the Old Testament.

Nicolas Bourbon devoted himself to Latin poetry, and in this field was praised by Paul Jove and Sainte-Marthe, but Scaliger called him a poet without name and of no importance. The list of his works includes a half dozen items, most important of which is the "Nicolai Borbonii Vandoperani Lingonensis Nugarum libri octo" published at Paris, and also at Basel in 1540. Joachim de Belluy, in his "Délices des poëtes françois," gives this epigram on the title of "Nugae" used by Bourbon for his collection of poems:

> Paule, tuum inscribis Nugarum nomine librum,
> In toto libro nil melius Titulo.

(Paulus, you entitle your book "Trifler"; in the whole book there is nothing better than the title.)

Ouwen also made a jest about it:

> Quas tu dixiste nugas non esse putasti;
> Non dico nugas esse sed esse puto.

(You believed that the writing, which you declared "trifles" were not trifles; I do not say they are trifles but I consider them as such.)

"*Παιδαγωγεῖον*, sive puerorum morbis libellus, apud Philippum Rhomanum Lugduni," 1536, was so highly esteemed by Jean des Caures d'Amiens, usually called Colletet, that he reissued the poem in Paris, 1571,

The poet Nicolas Bourbon de Vandeuvre. Drawing in black and colored chalk in the Library at Windsor Castle. Reproduction after a photograph by Franz Hanfstängl, Munich, in Knackfus's "Holbein." Courtesy of Velhagen and Klasing, Leipzig.

with comment of his own. In addition, it was issued in 1538, "apud seb Gryphium, Lugduni." The 1536 edition is to be found in the British Museum and the Bibliothèque Nationale in Paris. It is a little quarto of forty-four pages of which some ten are taken up with "Carmen de moribus, cui titulus *Παιδαγωγεῖον*." It is a very pious poem and is followed by some graces for table, epitaphs and the like in which the author calls himself poet laureat.

One of the prayers, "To Boys," may be quoted:

I entreat all boys who have read this little book to interpret it favorably, to pray for the King, for his family, for our native land, for Gaul, for all people, for me, that I may diligently and successfully benefit liberal studies. Prayers which come from pure and faithful hearts have much power with God.

NICOLAI
BORBONII VANDO-
PERANI OPVSCVLVM
PVERILE AD PVE-
ROS DE MO-
RIBVS,
SIVE
ΠΑΙΔΑΓΩΓΕΙΟΝ.
VIRTVTE DVCE,
COMITE FORTVNA.
PARISIIS APVD SEB.
GRYPHIVM,
1536.

Title page of Bourbon's pediatric contribution.

Bourbon complained somewhat bitterly that:

In my youth I lived in squalor;
Now a wealthy old man, I am languishing.
When I could enjoy riches I was wretched;
When I cannot enjoy them, lo! I am wealthy.

The poem itself is not an important contribution to pediatrics in any sense, but it is interesting as a rare specimen of teaching the subject in verse, and his views of education are not without merit. His opinion of the cause of tantrums in stubborn children is in accord with the present day ideas on the subject. This has been chosen to illustrate his style, a few lines of the original and the page as rendered by Miss Ruth Gilroy:

Luceat, hoc Christus, gloria nostra, jubet,
Praeterea est ratio sermonis habenda: loquendo
Ne lingua improbula garrulitate fluat.
Nec sint, qui bulbis feriant mihi naribus aures,
Quicque fremant, stridant, & male verba sonent,
Felix ingenium pulchras se praebet ad artes:
Calcitrat infelix, indomitumque furit.

The last two lines might serve as a good motto for the pediatric psychologist. The translation is as follows:

Christ, our glory, commands your moderation to shine forth everywhere, both day and night. Moreover, the manner of speech must be considered: in speaking, let not the tongue run on in somewhat wicked garrulity. May there not be those who din our ears by speaking through the nose, who mutter, hiss, and pronounce their words incorrectly. *The happy disposition behaves in an honorable manner; the unhappy one is stubborn, and the ungoverned rages.* There are fruits which grow mellow, just as wax, when brought near the fire; there are things which become hard, like clay. The hearts of boys are easily persuaded by words, but I grieve at those which become hard. Do not fear the rod and switches unless you offend; lashes are suitable for the bad, but sweetmeats must be given to the good. I hate the Orbilii who blunt and scourge the spirits which they should calm. The wise teacher understands and is anxious to correct the faults of natural disposition, and controls fierce hearts. Unhappy is he who perceives too late that he is an idle old man; unhappy also is he of whom people say: "this boy did not lack natural ability, nor the concern of a teacher, nor wealth, nor opportunity; he neglected his own advantages." The earth, if it has been well tilled, gives so many flowers; good fruits, and healthful herbs,—so many treasures. What would my Vandeuvre-du-Poitu and my native Langres be now, had it not been for the cultivation of the land?

News and Comment

GENERAL

Children's Clinic, College of Medicine of Strasbourg.—A postgraduate course in pediatrics will be organized under the direction of Professor Rohmer, at the Children's Clinic of Strasbourg from Oct. 10 to 22, 1932, with the following program: (1) Alimentation, Nutrition and Digestive Disorders of the Nursling, Professor Rohmer and Dr. Woringer. (2) Older Children: Tonsillectomy, Professor Canuyt; Mental Deficiency, Professor Pfersdorff; Ocular Lesions in Hereditary Syphilis, Professor Weill; Disturbances of Physical Development in Children, Alimentation of Older Children and Dyspepsia and Chronic Enteritis after the First Year, Professor Rohmer; Acetonic Vomiting, Treatment of Nephritis and Neuroses in Children and Indications and Results of Blood Transfusion in Children, Dr. Phelizot; Intestinal Occlusion, Dr. Bindschedler; Rôle of Latent Infection in Diseases of Children, Dr. Woringer. (3) Infectious Diseases: Serotherapy, Dr. Willemin-Clog; Tuberculosis and Hereditary Syphilis, Dr. Vallette. (4) Social Work, Professor Rohmer. The conferences will take place daily from 9 to 10, 11 to 12 and 5 to 6 o'clock. A clinical visit, with examination of patients, will occur daily, from 10 to 11 a. m. From 3 to 5 p. m. there will be demonstrations and practical work in the laboratory and nursery and inspection of children's institutions. The enrollment fee is 300 francs. For enrollment and all information address Professor Rohmer, Directeur de Clinique Infantile, Hôpital Civil, Strasbourg.

Bequests and Donations.—St. Mary's Free Hospital for Children, New York, was given $50,000 by the will of the late Edward B. Sexton.

St. Mary's Hospital for Children and Stuyvesant Square Hospital, New York, received $16,837 each, and St. Luke's Hospital, $10,103 by the will of Mrs. Hannah M. Lydig.

Southern Pediatric Seminar.—The Seminar was held at Saluda, S. C., from July 26 to August 6, under the direction of Dr. D. Lesesne Smith. Many prominent southern pediatricians give their services to this instructive course for practitioners.

UNIVERSITY NEWS

Changes in the university chairs of pediatrics in Italy are as follows: Prof. Vittore Zamorani has been appointed to the University of Pavia; Prof. Giuseppe Macciotta to the University of Cagliari, and Prof. Bruno Trambusti to the University of Parma. Prof. Olimpio Cozzolino has left the University of Parma for University of Bari. Prof. Angiola Borrino goes from the University of Sassari to the University of Perugia. Prof. Gian Carlo Bentivoglio has been placed in charge of pediatrics at the University of Sassari.

Rockefeller Foundation has granted Western Reserve University $25,000 for a four-year study of whooping cough under the direction of Dr. Gerald Shibley.

PERSONAL

Oscar M. Schloss has been appointed pediatrician-in-chief of the New York Hospital. He will head the Children's Hospital at the new medical center and will give full time.

Abstracts from Current Literature

Pathology, Bacteriology and Biochemistry

THE HYPOGLYCEMIC ACTION OF THE HYPOPHYSECTOMIZED DOG'S BLOOD. R. J. COWLEY, J. Pharmacol. & Exper. Therap. **43**:287 (Oct.) 1931.

The author gives a brief summary of the relationship between the hypophysis and carbohydrate metabolism from the experimental and clinical data to date. He found that blood from hypophysectomized dogs given subcutaneously lowered the blood sugar of rabbits more than did the blood of normal dogs. This result is considered to depend on an increase in a hypoglycemic, insulin-like substance, or a decrease in a hyperglycemic substance.

PILCHER, Cleveland.

CONTINUED DRINKING OF ALCOHOL IN LOW CONCENTRATIONS: SOME EXPERIMENTAL RESULTS. P. J. HANZLIK, J. Pharmacol. & Exper. Therap. **43**:339 (Oct.) 1931.

The voluntary drinking of alcohol in animal experimentation has not been reported. Pigeons voluntarily drank diluted alcohol (from 2 to 4 per cent) during periods of from thirteen to twenty-four months, at times showing gross evidence of intoxication. The author's conclusions are in part as follows: "The essential results indicated a loss of body weight from which recovery was slower than in the controls, despite the large number of calories obtained from the alcohol; cultivation of appetite for alcohol; possible species preference for 2 per cent alcohol; no significant change in food consumption; and no demonstrable gross and histological changes in the heart, kidneys and liver, the latter confirming the negative results of others using stronger alcohol in other animals. From the results obtained, it is tentatively suggested that the continued use of weak alcohol does not act as food or stimulate appetite for, or the consumption of, food, since it does not restore or maintain body weight, thus acting in this sense as a poison, but that injury to viscera is not demonstrable after drinking weak alcohol for about one-seventh to two-sevenths the span of life. Hence, the other constituents of weak alcoholic beverages may be responsible for the clinical effects on vegetative functions and on viscera."

PILCHER, Cleveland.

THE DEGREE OF INFECTION IN RELATION TO THE PARASITICIDAL ACTIVITY OF CHEMOTHERAPEUTIC COMPOUNDS. JOHN A. KOLMER, J. Pharmacol. & Exper. Therap. **43**:521 (Nov.) 1931.

Rabbits' testicles were given injections of Spirochaeta pallida; rats were inoculated intraperitoneally with Trypanosoma equiperdum. The author found in treatment that spirocheticidal and trypanocidal agents were more effective in the presence of early light infections than when they were given as abortive treatment immediately after inoculation.

PILCHER, Cleveland.

CALCIUM AND PHOSPHORUS REQUIREMENTS FOR GROWING CHICKS: I. STUDIES WITH SALT MIXTURES UNDER RACHITIC CONDITIONS. W. C. TULLY, S. M. HAGUE, C. W. CARRICK and ROY E. ROBERTS, Poultry Sc. **10**:299, 1931.

McCollum's mineral no. 185 (composed of sodium chloride 0.173 Gm., magnesium sulphate 0.266 Gm., disodium acid phosphate 0.347 Gm., dipotassium acid phosphate 0.954 Gm., monocalcium phosphate 0.540 Gm., iron lactate 0.118 Gm. and calcium lactate 1.300 Gm.) and substitutions of calcium salts in it to produce a wide variation in the calcium: phosphorus ratio, when used with a semipurified

ration in the absence of vitamin D, did not result in satisfactory growth or proper formation of bone in chicks, but with the addition of vitamin D the chicks approached optimal growth. Good growth was not obtained in young chicks fed a mineral mixture composed chiefly of dicalcium phosphate at the level at which it was used in the semipurified ration, either with or without an adequate supply of vitamin D in the form of irradiation.

KUGELMASS, New York.

THE WATER CONTENT OF ORGANISMS UNDER NORMAL AND PATHOLOGIC CONDITIONS. MARGARET ESSER, Schweiz. med. Wchnschr. **62**:61 (Jan. 16) 1932.

The author records a series of analyses on various human organs, normal and diseased, for water and chloride content. The variations of her findings were:

	Water, Per Cent	Chloride, Mg. per 100 Cc.
Liver	68–78.0	185–242
Bile	81–91.5	163–344
Spleen	74–86.0	185–256
Kidney	74–82.0	178–253
Brain, gray matter	81–87.0	353–725
Brain, white matter	69–81.0	232–298
Stool	60–80.0	

In skin from various parts of the body of the same subject the water content varied from 45.1 to 65.1 per cent. Rats were killed after being kept for twelve days on diets that were normal, dry and rich in water. Little variation was noted in the water content of skin, kidney and bone, but the percentage in the liver was lower in the dry animals than in the controls. Frogs kept for several days in high concentrations of salt solution had a higher water content than their controls. Rats poisoned with mercury cyanide, a diuretic, lost water from muscles, liver and kidneys, but their skin content remained unchanged.

WOLMAN, Chicago.

THE DISTRIBUTION OF AMINO-ACIDS IN THE BLOOD IN ANEMIA. SANDOR SIMON, Magyar orvosi arch. **32**:202, 1931.

A study was made of the distribution of amino-acids between corpuscles and plasma of normal and of anemic human and animal bloods. The colorimetric method of Folin was used. In anemia the amino-acid content of red blood cells is either high or normal (with maximal figures). The ratio of corpuscle amino-acid to plasma amino-acid is always increased in anemia. The amino-acid contents of plasma and whole blood are unchanged. During the time of regeneration the ratio of corpuscle amino-acid to the plasma and whole blood amino-acid decreases. The organism shows a tendency to distribute amino-acids at the same rate between plasma and corpuscles.

KUGELMASS, New York.

Nutrition

THE SEDIMENTATION VELOCITY OF BLOOD CELLS IN EYE DISEASES CAUSED BY VITAMIN A DEFICIENCY. I. JOHN, Am. J. Ophth. **14**:590 (July) 1931.

This is a contribution to the knowledge of systemic changes in the human body caused by vitamin A deficiency. Twenty-three adults were studied and the following conclusions made: 1. The blood sedimentation test was done in twenty-two patients with diseases due to vitamin A deficiency; seven of them suffered from keratomalacia and fifteen from xerotic changes in the eye of different degrees of severity, one patient having only hemeralopia. 2. Six of the patients with keratomalacia showed normal sedimentation figures. 3. Eight of the fifteen patients with xerosis also showed normal sedimentation figures. 4. The increased figures in seven cases of xerosis must be attributed to complications caused by other

diseases, because the sedimentation figures, even after healing of the visible changes of the eye following treatment with cod liver oil, showed also pathologically increased sedimentation velocity. 5. The sedimentation velocity of the cases of keratomalacia increased after starting treatment with vitamin A.

REESE, Philadelphia [ARCH. OPHTH.].

PRENATAL CARE AND FEEDING IN RELATION TO DENTISTRY. ELIOT BISHOP, Dental Cosmos **74**:41 (Jan.) 1932.

The author emphasizes the fact that during pregnancy and lactation there is a drain on the calcium reserves of the mother. The blood calcium falls during pregnancy and drops more at the end of pregnancy, as a result of the requirements of the developing fetus. Phosphorus is another element necessary for proper osseous structure. The author feels that the diet that he prescribes contains these two elements in sufficient amount. Should symptoms of calcium deficiency appear, he increases the intake by means of syrup of calcium lactophosphate. The diet containing calcium and phosphorus is composed of milk, cheese, egg yolk, spinach, celery, lettuce, greens, fruits, whole wheat, coarse corn, buckwheat, peas and beans. Should there not be sufficient retention of calcium, there is evidently a lack of vitamin D, which can be supplied by means of cod liver oil or viosterol.

MARKUS, Philadelphia.

RELATION OF METABOLISM TO DENTITION. CARL P. SHERWIN, Dental Cosmos **74**:45 (Jan.) 1932.

The author states that an adequate or proper diet is sufficient to maintain a healthy body, and is absolutely a necessity for the maintainance of a body to resist disease. In a healthy body with proper or adequate diet, good teeth are the natural sequence. A proper diet should meet the following requirements: It should furnish sufficient energy (about 3,200 calories for the average adult); it should be apportioned properly among carbohydrates, proteins, fats, water, minerals and oxygen; it should also have a sufficient amount of roughage (cellulose), and it should be palatable, clean and result in an alkaline ash. Proper protein should contain the following essential amino-acids: lysine, cystine, trytophan and histidine. Should these be absent, there is a failure to grow. Lipoids are essential and should be supplied in abundance by means of the following foods: glandular foods, bone marrow, brain and yolk of egg. Fats are also essential, and can be derived from butter, cream and the fat of meats. Vitamins A and D are necessary for normal teeth and the periodontal tissues. It is essential that they be supplied in early life during development, for if they are absent at that time, poor dental tissues will result, even if the vitamins are supplied later.

MARKUS, Philadelphia.

PELLAGRA: PREVENTATIVE VALUE OF CERTAIN CANNED VEGETABLES. G. A. WHEELER, Pub. Health Rep. **46**:2663 (Nov. 6) 1931.

Canned turnip greens supply the pellagra-preventive vitamin, and in liberal quantities supplement an otherwise pellagra-producing diet. Canned spinach supplies some of the vitamin, but is not especially rich in it. Canned green beans are a relatively poor source, and the mature onion is a very poor source.

SANFORD, Chicago.

GUANIDINE AS A TOXIC SUBSTANCE IN THE BLOOD OF INFANTS FOLLOWING ACUTE DEHYDRATION. HORTON CASPARIS, South. M. J. **25**:147 (Feb.) 1932.

The author calls attention to the fact that the treatment of infants who are severely sick as a result of marked loss of fluid and salt resulting from acute gastro-intestinal disturbances has been somewhat discouraging, owing to the fact that severe symptoms often persist or new ones appear after corrective treatment

has been instituted. He points out the similarity of these symptoms to those seen in animals poisoned with guanidine. Determinations made on the blood of such sick infants showed very high levels of guanidine similar to the levels found in the blood of dogs poisoned with the drug. It has been observed that calcium administered to the toxic animals relieved them of their symptoms. In view of this fact, calcium therapy was made a part of the regular regimen of dehydrated sick infants. Calcium gluconate, in a dose of from 3 to 6 cc. of a 10 per cent solution, was given intravenously. The size of the dose varied with the size of the infant and the 10 per cent solution was diluted to about 1 per cent in other fluids. In addition to the diluted intravenous solution, 5 or 10 cc. of an undiluted 10 per cent solution was given intramuscularly. The author is under the impression that definite improvement results from this treatment.

SCHLUTZ, Chicago.

SOME EFFECTS OF A KETOGENIC DIET. RICHARD W. B. ELLIS, Arch. Dis. Childhood **6**:285 (Oct.) 1931.

Twenty children between the ages of 3 and 8 years were put on a ketogenic diet, with the purpose of testing tolerance to a diet with a high fat content in various conditions. Artificially produced ketosis before and after operation was well tolerated. In cyclic vomiting and convulsions at the onset of acute infection, a ketogenic diet produced no symptoms. The majority of patients lost or failed to gain weight during the feeding of a ketogenic diet. It is not claimed that ketosis can never be responsible for clinical disturbances, since in extreme degrees considerable change in the acid-base equilibrium may take place. It is, however, suggested that a considerable ketosis may be well tolerated by many children, including certain "cyclical vomiters" and normal children undergoing operation. It follows that a diagnosis of "ketosis" as an explanation of symptoms should be made only with the greatest caution and when every other possible cause has been excluded. This is of additional importance when it is remembered that the prolonged administration of dextrose in considerable quantity may result in the precipitation of diabetes in a subject in whom pancreatic function is defective.

KELLY, Milwaukee.

ALKALOSIS IN THE VOMITING OF INFANCY. MONTAGUE MAIZELS, Arch. Dis. Childhood **6**:293 (Oct.) 1931.

Plasma bicarbonate, plasma and red cell chloride, the ratio of cell to plasma chloride and the hemoglobin content were investigated in vomiting infants. The cases were divided into two groups: (1) obstructive vomiting, pyloric stenosis or spasm, and (2) habitual vomiting and that due to feeding. There were seventy-three cases in group 1 and forty-seven cases in group 2. In pyloric obstruction there was a marked increase of plasma bicarbonate with a decrease of the plasma and red cell chlorides. One or more of these changes occur in 88 per cent of all cases and have a positive diagnostic significance. Alkalosis or marked reduction of chloride is rare in nonobstructive vomiting.

After the therapeutic administration of physiologic solution of sodium chloride and dextrose (from 15 to 20 ounces [425.2 to 566.9 Gm.] over a period of forty-eight hours), as a rule, the alkali reserve decreased, the plasma and red cell chloride and the ratio of cell to plasma chloride rose, while the hemoglobin and hematocrit reading fell owing to the retention of water in the circulation. In many cases, the fall in the hematocrit reading was much less marked than the fall in hemoglobin, indicating that relatively more water was retained in the red cell than in the plasma. In one third of the cases, all the changes resulting from treatment were present simultaneously. In the other cases one or more of these changes were absent. The alkali reserve showed a marked fall in 56 per cent of cases, and this fall was accompanied by a corresponding rise in the chloride.

KELLY, Milwaukee.

SCURVY IN NATIVE CHILDREN. SHENA ROSS, J. M. A. South Africa **5**:596 (Sept. 26) 1931.

A severe and prolonged drought in 1927 and 1928 was responsible for the development of numerous cases of scurvy in the native inhabitants of the Ciskeian area of the Cape Province of South Africa. The diet of many young children was reduced to maize porridge, maize water or maize itself. Of the 208 patients with scurvy admitted to the Victoria Hospital at Lovedale, there were 36 children between the ages of 4 and 14, and 77 between the ages of 1 and 3 years. The most striking feature of the disease in the children was the occurrence of extreme edema of the legs, arms, face, external genitalia and dependent portions of the trunk. In severe cases the edema was so intense in places as to cause breaking down of the overlying skin. Hemorrhage, although present, was never a marked sign. "Dysenteric diarrhea" was present in almost all cases. Fever was generally present. Bronchitis and bronchopneumonia were frequent complications. All symptoms and signs, including those of the respiratory complications, cleared up rapidly following the administration of lemon juice.

GONCE, Madison, Wis.

DWARFISM AND RICKETS. BERNARD SCHLESINGER, Proc. Roy. Soc. Med. **25**:10 (Nov.) 1931.

A case of dwarfism and rickets was reported in a boy of 7 years. At 10 months of age his foot was noticed to be turned in, and he was treated for rickets for some time, without improvement. Albuminuria was first noticed at the age of 4 years. The deformities progressed, and the child began to complain of thirst and polyuria. On examination he weighed 32 pounds (14.5 Kg.). His height was 37 inches (93.9 cm.). He showed marked genu valgum and enlarged epiphyses of the arms and legs. The serum calcium content was 9.7 mg.; the inorganic phosphorus, 1.7 mg., and the blood urea, 36 mg. per hundred cubic centimeters. The Wassermann reaction was negative.

WILLIAMSON, New Orleans.

CHLORINE IN EXPERIMENTAL SCURVY. A. MICHAUX, Bull. Soc. scient. d'hyg. aliment. **19**:117, 1931.

Experiments are described which show that the antiscorbutic vitamin exerts an undoubted effect on chlorine metabolism, a deficiency of this vitamin producing, after a variable period, considerable retention of chlorides, the effects of which are manifested not only in the blood but also in the muscular tissues. On the other hand, the addition of a food containing this vitamin to a diet relatively rich in sodium chloride contributes to the maintenance of a normal chlorine content in the blood and muscles by increasing the amount eliminated.

KUGELMASS, New York.

AVITAMINOSIS. R. DUBOIS, Nourrisson **19**:337 (Nov.) 1931.

It has been demonstrated experimentally that animals on a diet totally or partially deficient in vitamins have a lowered resistance to infections. Deficiency diets for animals can be adjusted to produce varied symptoms, depending on the degree of vitamin deficiency. The same is true in infants. Withholding vitamin C entirely, one will produce an acute scurvy, but if the diet contains only an inadequate amount of vitamin C such indefinite symptoms as failure to gain in weight, anemia, angiodystrophy and a lowered resistance to infections may alone be present. Suboptimal amounts of vitamin A or B may occasion a similar train of symptoms. These symptoms promptly disappear when the deficient vitamins are supplied in adequate amounts. Data are also presented to show that infants deprived of vitamins in adequate amounts are easy prey to many acute and chronic

infections, such as parenteral dyspepsia, pyelitis, pyodermia, recurrent infections of the upper air passages, otitis, bronchitis and even bronchopneumonia. Numerous illustrative cases are cited. It is important that these infants receive all the vitamins, even during the acute stage of illness.

McCLELLAND, Cleveland.

THE ULTRA-RED ABSORPTION SPECTRUM OF ERGOSTEROL AND ANTIRACHITIC SUBSTANCES. WALTER HIRSCH and LOTTE KELLNER, Biochem. Ztschr. **235**:162, 1931.

Ergosterol has only one absorption band in the ultra-red spectrum at 3.71 microns, while antirachitic substances have in addition to this a weaker second band at 0.97 microns, i. e., near the visible spectrum. Besides, the antirachitic substances have a greater absorption than the ergosterol. In all probability one is dealing here with a large number of absorption bands which are fused because of the slight spread of the spectrum. Nevertheless, the difference in the ultra-red spectrum of biologically active and inactive ergosterol is sufficiently striking to serve as a means of differentiation between the two forms, and is especially useful for such concentrated solutions as viosterol, which is opaque to ultraviolet radiations.

KUGELMASS, New York.

THE USE OF FAT, ESPECIALLY GOOSE FAT, IN INFANT FEEDING. HERBERT KOCH, Kinderärztl. Praxis **2**:159 (April) 1931.

Koch has used goose fat in infant feeding for the past year. It is prepared with flour, similarly to the Czerny-Kleinschmidt butter-flour mixture. It is indicated in all cases of chronic malnutrition but never in acute nutritional disturbance. The author recommends it for its digestibility, its nutritional value, its cheapness and because it keeps well.

HUENEKENS, Minneapolis.

VEGETABLE AND RAW DIET FOR CHILDREN. EMIL FEER, Kinderärztl. Praxis **2**:162 (April) 1931.

Feer restricts infants under 6 months of age to 500 cc. of cow's milk per day. After that age he cuts this amount down to 300 or 400 cc. After one year the diet should be rich in vegetables, potatoes, whole bread and butter and raw fruits; raw vegetables may be given. Milk, eggs and meat should be given in small quantities.

HUENEKENS, Minneapolis.

THE APPEARANCE OF NICOTINE IN BREAST MILK AFTER CIGARET SMOKING. WILHELM EMANUEL, Ztschr. f. Kinderh. **52**:41, 1931.

After the smoking of seven or more cigarets nicotine was found in the milk as well as in the urine. The greatest concentration occurred four or five hours after smoking.

SHELLING, Baltimore.

SERUM MAGNESIUM CONCENTRATION IN EXPERIMENTAL RICKETS AND HYPERVITAMINOSIS D. CHRISTIAN BOMSKOV and ERNST KRÜGER, Ztschr. f. Kinderh. **52**:47, 1931.

The magnesium concentration of the serum in rats rendered rachitic either by the McCollum diet or by thallium and also in those subjected to hypervitaminosis D is about 50 per cent of the normal. The authors suggest that the fall in the magnesium content of the serum is due to deposition of magnesium in the bones rather than to an increased excretion.

SHELLING, Baltimore.

THE ANTISCORBUTIC VITAMIN. J. TILLMANS, Ztschr. f. Untersuch. d. Lebensmitt. **60**:34 (July-Aug.) 1930.

For the differentiation of natural and artificial foodstuffs by measurement of the reduction potentials, 2, 6-dichlorophenolindophenol has been found extremely sensitive, and the presence of these reducing substances has been correlated with that of vitamin C. By titration with a solution of the dye it was found that the reducing material in lemon juice possesses a sensitivity toward heat, hydrogen and alkalis that is exactly parallel to that of the vitamin, while the titration of values of a large number of other foodstuffs agrees closely with the recorded content of vitamin C. An attempt has been made to isolate the reducing substance and the vitamin. That they are identical has not been confirmed.

KUGELMASS, New York.

SUGAR IN BABIES' DIET. R. C. P., Opieka nad dzieckiem **9**:217 (June) 1931.

Sugar is an important ingredient in the diet of babies because it gives energy and often takes the place of fat. In children who have poor appetite the addition of sugar to milk or soup often produces a miracle. In artificially fed babies sugar plays an important rôle if a half and half formula is used with 8.5 per cent sugar; if one part of milk and two parts of water are used, 6 per cent should be added. In England condensed milk is used considerably in feeding babies; in France, "lait du Poule." This milk is made by adding the yolk of an egg and 2 heaping teaspoonfuls of sugar to 8 ounces (236.6 Gm.) of hot milk.

KRUPINSKI, Chicago.

THE SIGNIFICANCE OF CONSTITUTIONAL INFLUENCES ON THE OCCURRENCE OF NUTRITIONAL DISTURBANCES IN BABIES. J. C. SCHIPPERS, Maandschr. v. kindergeneesk. **1**:55 (Nov.); 127 (Dec.) 1931.

In this investigation attention was paid especially to the significance of so-called constitutional hydrolability. A discussion is given of the expressions "constitutional" and "constitutional hydrolability." It is the author's opinion that from the conceptions of Finkelstein it followed that the greater number of children with severe nutritional disturbances were also hydrolabile before and after their recovery. In at least 25 per cent of a large number of cases of severe nutritional disturbances observed between 1914 and 1930, constitutional factors appeared to have played a rôle. In the remaining greater majority exogenic factors were the cause of the disease. Undoubtedly these figures will change greatly as conditions in Amsterdam have already changed. As regards hydrolability, the author is of the opinion that this often occurs as a diathesis, but that its significance for the etiology of nutritional disturbances as such is not great. As a symptom, however, it may be serious.

VAN CREVELD, Amsterdam, Holland.

THE GASEOUS METABOLISM IN CORPULENT CHILDREN. M. DE BRUIN, Nederl. tijdschr. v. geneesk. **75**:4418 (Aug. 29) 1931.

In fifteen corpulent children the basal metabolism was determined, and in ten of these also the specific dynamic effect of different articles of food. The basal metabolic rate was within normal limits. The specific dynamic effect was probably decreased in several cases. A preparation from the anterior lobe of the pituitary gland was given to five of the children. A clear effect of this preparation on the basal metabolism or a specific dynamic effect could not be demonstrated, though bodily and mental indolence was more or less favorably influenced.

VAN CREVELD, Amsterdam, Holland.

Prenatal Conditions

THE APICAL LOBE OF THE AZYGOS VEIN. G. CARRIÈRE, L. THOMAS and C. HURIEZ, Gaz. d. hôp. **104**:1333 (Sept. 5); 1365 (Sept. 12) 1931.

The authors give the anatomic description and the variations of the azygos lobe. In regard to etiology, they accept Dévé's view, that the anomaly is caused when the disappearance of the posterior cubital vein and the descent of the posterior cardinal vein (azygos) into the thoracic cavity do not occur simultaneously, the former exerting a pull on the cardinal vein which causes lateral displacement, so that the vein meets the outgrowing lung.

In order to differentiate this condition from enlarged mediastinal glands, they emphasize making roentgenograms in full expiration and inspiration. The so-called capillary line (caused by the fourfold pleura in the fissure) will be found widened in expiration.

KAJDI, Baltimore.

UNILATERAL CONGENITAL ABSENCE OF THE PECTORAL MUSCLES. P. PETRIDES, Rev. d'orthop. **18**:669 (Nov.) 1931.

In the January, 1931, number of *Revue d'orthopédie*, Aimes, Estor and Todorovitch reported a case of congenital absence of the pectoralis major. Petrides reports the complete absence of the pectoral group. His patient, the son of a physician, had some slight difficulty from birth (premature at eight months) in raising the left arm, but the parents did not notice any deformity. The general health was good, but the child was of a delicate constitution. Physical examination when 15 years of age did not show any abnormality except a loss of muscle tissue and some fibrous contraction of the anterior axillary fold. The left nipple was about 2 cm. higher than the right. The left arm could not be raised above 90 degrees because of the cicatricial skin of the anterior axillary fold. A Z incision was made through the skin, and the aponeurosis incised transversely almost up to the clavicle. The wound was closed with a small gauze drain to prevent the formation of hematoma. The results from the functional point of view were satisfactory.

RYAN, Vancouver, B. C.

ANOMALIES IN THE DEVELOPMENT OF THE VERTEBRAE. M. A. RECCANDTE, Rev. d'orthop. **18**:674 (Nov.) 1931.

The most frequent anomaly in the spine is a variation in the number of vertebrae. In 717 autopsies, 3.47 per cent showed an increased number, 0.66 per cent a diminution and 1.1 per cent an irregularity in distribution of the vertebrae.

Embryologically, the vertebrae commence to ossify at the end of the second fetal month. There are three centers of ossification; two of them develop into the arcs, and the third forms the body. This center for the body arises as two separate centers, which become fused. Many authorities believe that the development of the ribs is intimately connected with the development of the vertebrae. Reccandte agrees with this hypothesis, because in the case that he reports, the second dorsal vertebra is incompletely developed on the right side and the corresponding rib is absent; proof that the rib is developed as a prolongation from the lateral center for the arc.

The etiology of the maldevelopment in this case may have been influenced by two factors; the child was born during the period of famine and distress following the war, when wheat flour had to be replaced by substitutes, and there may have been some interference with the development of the blood supply to the vertebrae.

RYAN, Vancouver, B. C.

GIGANTISM. FRANCISCO A. DELUCA, Arch. am. de med. **8**:19 (Jan.) 1932.

The author reports a case of gigantism in an infant whose weight at birth was 6,630 Gm. The infant was born dead. In connection with this case, the

author reviews the experience in one of the large maternity hospitals in Buenos Aires. In a series of 34,019 births extending over a period of seventeen years, 69 cases of gigantism occurred. The larger proportion of them were in males. In 35 of the cases the birth was normal, in 34, abnormal. In 5 of the cases rupture of the uterus occurred. Only one patient was delivered by cesarean section. In 21 cases the infant was born dead, and the condition was fatal to the mother in 3 cases.

SCHLUTZ, Chicago.

CONGENITAL GENITAL PROLAPSE. SUPRAVAGINAL AND INTRAVAGINAL HYPERTROPHY OF THE CERVIX UTERI. OTHER MALFORMATIONS. VICTOR RAGGIO and JUAN VIZZIANO PIZZI, Arch. de pediat. d. Uruguay **2**:388 (Aug.) 1931.

The patient whose case is reported was the offspring of an alcoholic father. The birth weight and height were normal. She presented bilateral genu recurvatum, bilateral equinus clubfoot, congenital subluxation of both hips, sacral spina bifida and vaginal and supravaginal hypertrophy of the cervix of the uterus with considerable prolapse of this organ.

SCHLUTZ, Chicago.

A CASE OF CONGENITAL ATRESIA OF THE VALVE OF BAUHIN. A. WILKE, Jahrb. f. Kinderh. **134**:10 (Dec.) 1931.

This is the report of a case with autopsy. The gross but not the microscopic examination is fully presented. Maldevelopment and not inflammation appeared to be the causative factor.

CLAUSEN, Rochester, N. Y.

EPIGASTRIUS PARASITICUS. KARL SEYNSCHE, Jahrb. f. Kinderh. **134**:40 (Dec.) 1931.

The author presents a complete review of the literature and the description of a case. The parasitic monster was successfully removed by operation on the third day. The host was apparently healthy at the age of 3½ months.

CLAUSEN, Rochester, N. Y.

CONGENITAL SHORTNESS OF ESOPHAGUS, COMBINED WITH THORACAL STOMACH AND WITH CARDIOSPASM. A. BROWN-KELLY, Monatschr. f. Ohrenh. **65**:1369 (Nov.) 1931.

Brown-Kelly thinks that congenital shortness of the esophagus would perhaps not prove to be as rare as is commonly believed if the symptoms were better known. In describing the symptomatology, he mentions as the most outstanding symptom the so-called vomiting, which is largely due to regurgitation. The largest portion of the article treats of the methods of examination, especially of roentgenoscopy and of endoscopic examination, that are necessary for recognition of the condition. In regard to the treatment, the author states that neither a congenitally short esophagus nor the resulting thoracal stomach necessitates surgical intervention. The cardiospasm, however, should be treated by dilatation of the cardia.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

CONGENITAL ATRESIA OF THE DUODENUM WITH DUPLICATION OF BILE AND PANCREATIC DUCTS. K. KATZ, Virchows Arch. f. path. Anat. **278**:290, 1930.

Atresia of the duodenum in a child that died on the seventh day after birth was associated with duplication of the distal portion of the ductus choledochus and of the pancreatic duct. One bile duct and a pancreatic duct entered the duodenum above the atresia; the other pair, below the atresia.

SCHULTZ, Chicago. [ARCH. PATH.]

CONGENITAL ATRESIA OF THE TRANSVERSE COLON. H. POPPER, Virchows Arch. f. path. Anat. **278**:295, 1930.

Congenital stenosis and atresia of the intestinal tract occur most frequently in the anus and rectum and next most frequently in the duodenum. The condition is seen less often in the jejunum and lower end of the ileum and least frequently in the colon. In the case presented, that of a stillborn, full-term infant, the ascending colon was greatly enlarged and ended blindly. It was not normally attached to the lateral body wall and the blind end lay in the left iliac fossa. The transverse colon was represented by a narrow cord, 8 cm. long, in the border of the transverse mesocolon. Microscopic examination revealed no intestinal tissue in this cord. The blind end of the distal colon was situated at the lower pole of the spleen and corresponded to the splenic flexure. The rectum was also atretic. In his discussion of the mechanism of the conditions found, the author devotes chief attention to the enlargement of the blind ascending colon. The enlargement was not due entirely to simple mechanical distention, but in part at least to marked hypertrophy of the wall. The author believes that the anomaly described was the result of two simultaneous errors of development. One was hypertrophy and overgrowth of the ascending colon, similar to the process that leads to congenital megacolon of Hirschsprung. The other was an inhibition of development that led to atresia of the transverse colon and rectum.

SCHULTZ, Chicago. [ARCH. PATH.]

CONSTITUTIONAL VARIATIONS IN CRANIAL FORM AND OXYCEPHALY. H. GÜNTHER, Virchows Arch. f. path. Anat. **278**:309, 1930.

Günther presents measurements of a number of variations in cranial form that he believes to be dependent on constitutional factors, and discusses the variations in relation to oxycephaly, for which he prefers the name akrocranium. Oxycephaly, which is due to hypoplasia or retarded development of the base of the skull, is often merely a subjective impression. Substantiation of this impression requires deviation from normal cranial measurements and indexes of a definite order of magnitude. Most important are the measurements and indexes that express the relationship of cranial circumference to height. Two pure types of akrocranium are recognized, one with, the other without, exophthalmos and angular deformity of the maxilla. The cranial deformity is often associated with impairment of vision (akrocraniodysopia), increased fragility of the erythrocytes and hemolytic icterus (akrocraniodyshemia) and phalangeal abnormalities (akrocraniodysphalangia). Although the cranial deformity may be due to mechanical factors acting on the fetus after development has been initiated, in which case the deformity is an acquired one, in the majority of instances the deformity is the result of abnormalities in the genetic constitution of the germ plasm. The associated abnormalities Günther also believes to be constitutional in nature.

SCHULTZ, Chicago. [ARCH. PATH.]

CONGENITAL MALDEVELOPMENTS: ATRESIA OF THE SMALL INTESTINE. G. BODON, Virchows Arch. f. path. Anat. **278**:529, 1930. VENTRAL HERNIA. Z. SZANTROCH, ibid., p. 539. MALDEVELOPMENTS OF THE CEREBELLUM. H. TESSERAUX, ibid., p. 555. COMPLETE AND UNILATERAL ABSENCE OF VERTEBRAL BODIES. A. FELLER and H. STERNBERG, ibid., p. 566.

Four successive contributions are devoted to examples of congenital maldevelopments of the types indicated by the titles. Each reviews the theories that have been propounded in explanation of the genesis of the particular anomaly and attempts to interpret the latter in the light of these theories.

SCHULTZ, Chicago. [ARCH. PATH.]

INVESTIGATIONS OF THE TRANSMISSION OF NITROGEN-CONTAINING SUBSTANCES FROM FETUS TO MOTHER. JOHN NAESLUND, Acta obst. et gynec. Scandinav. **11**:474, 1931.

The author gives the results of investigations into the protein and water content of the serum, fibrinogen, nonprotein nitrogen, xanthoprotein, creatinine, uric acid and amino-acid concentration in the blood of mother and child.

The nonprotein nitrogen was determined in forty-one cases, all of which showed that it was less in the mother's blood at the time of delivery than in that of the fetus, and in the latter it was less in the umbilical vein than in the artery.

The nonprotein nitrogen in the fetal blood is not constant, but varies more or less with fluctuations in maternal blood. No correspondence between the nonprotein nitrogen content and the serum protein concentration could be ascertained. In cases of nephropathy, the nonprotein nitrogen content was high, especially in the fetus. In one case it was 80 mg. per cubic centimeter in the maternal, and 84 mg. in the fetal blood.

The xanthoprotein values were determined in forty-five cases, and were found to be higher in the fetus than in the mother. The difference between the two is quite constant, being about one-third higher in the fetus. The xanthoprotein values were higher in the umbilical arteries than in the veins. Cases of nephropathy exhibit higher values than normal in the mother but not in the fetus.

The author believes that the xanthoprotein substances are formed in the fetus without bacterial decomposition and are passed to the mother.

The creatinine content was studied in twenty-six cases. In five, the parturients were given injections of from 0.5 to 1.5 Gm. of creatinine, which increased the content of the maternal blood greatly. There was no increase in the creatinine content of the fetal blood within the first half hour; in about two hours it was raised, but it was never increased to the value in the maternal blood. In the remaining twenty-one cases, the creatinine content was regularly higher in the fetal than in the maternal blood, and the difference is constant. The value is usually higher in the arterial than in the venous fetal blood. Labor seems to increase the values. The nonprotein values seem to rise with those of creatinine.

The uric acid content was investigated in forty-one cases, and in four of these, sodium chloride was injected in doses of from 0.5 to 1 Gm. An increase in uric acid was found in the mother's blood within from ten to fifteen minutes after injection. There was no unmistakable increase in the fetal blood within one-half hour, though in one case it was marked after two hours.

In the thirty-seven cases there were variations; in some the values were the same, in others they were lower, and in still others they were higher in the fetal than in the maternal blood.

The values for uric acid are high in the nephropathies in the maternal but not in the fetal blood.

The mean value of uric acid is somewhat higher in the primipara than in the multipara. There seems to be a certain agreement between the values of uric acid and those of nonprotein nitrogen. The concentration of amino-acids was studied in thirteen cases. The values were much higher in the fetal than in the maternal blood. There was no constant relationship between the amino-acid and the nonprotein nitrogen values. The amino-acids are not to be regarded as waste products of nitrogen metabolism as are other nonprotein nitrogenous substances.

ADAIR, Chicago.

Diseases of the New-Born

PEMPHIGUS NEONATORUM CONGENITUS OR IMPETIGO NEONATORUM CONGENITA. CHARLES D. FREEMAN, Arch. Dermat. & Syph. **24**:1058 (Dec.) 1931.

In the author's review of the literature he questions the authenticity of most of the cases of pemphigus neonatorum congenitus reported. The congenital occurrence of this disease is rare. Most cases develop after birth and cannot be termed congenital.

Two cases are reported that showed typical bullae at birth. In two members of one family and in one member of the other impetigo contagiosa developed after contact with these infants. This shows that the congenital form when unrecognized may be the source of origin of epidemics. The mothers of these two patients were well during the antepartum period and did not contract the disease.

The streptococcus is considered to be the causative factor. There is still a question as to how the infection reaches the infant.

HENNING, Iowa City.

THE SYNDROME OF ADRENAL HEMORRHAGE IN THE NEW-BORN. M. A. GOLDZIEHER and M. B. GORDON, Endocrinology **16**:165 (March-April) 1932.

Excluding cases in which no clinical data were available, the authors were able to collect from the literature seventy-five cases of suprarenal hemorrhage in infants and children, to which they added six additional instances. These eighty-one cases form the basis of this study.

The suprarenal gland is probably the most vascular organ during the neonatal period and is extremely friable. Immediately after birth a process of involution takes place in which the reticular and trabecular layers are destroyed and replaced by highly vascularized, fibrillar connective tissue. Such a degree of hyperemia is conducive to hemorrhage. The etiologic factors are: (1) those related to labor (trauma during birth, asphyxia neonatorum, trauma due to artificial resuscitation and eclampsia in the mother), (2) local conditions (physiologic involution of the suprarenal cortex, stasis due to compression of the vena cava between the liver and the vertebral column and thrombosis of the suprarenal vein) and (3) general conditions (hemorrhagic diathesis, acute infections and syphilis).

The authors feel that, on the basis of recent experimental evidence, an analysis of the eighty-one cases in the present study justifies the following classification of symptoms of suprarenal hemorrhage in the new-born.

1. Symptoms of acute suprarenal insufficiency. (*a*) Endocrine: rapid respiration, high temperature, rash (purpura or petechiae), metabolic changes, convulsions and cyanosis. (*b*) Associated symptoms: gastro-intestinal disturbances, such as vomiting, diarrhea and abdominal pain; nervous conditions, such as coma, convulsions and twitchings.

2. Symptoms of suprarenal hemorrhage. (*a*) General: shock and collapse; weak, irregular and small pulse; cold extremities; air hunger, and increasing pallor. (*b*) Local: Generally distended abdomen which gives a boggy sensation on palpation, abdominal pain, palpable tumor in the region of one or both kidneys and peritoneal symptoms with intraperitoneal hemorrhage.

The predominating symptoms in the order of their frequency are a high temperature, a cutaneous rash, rapid or irregular respiration, cyanosis, convulsions or twitching, vomiting, collapse, an abdominal tumor, jaundice and metabolic changes.

It is felt that three of these sets of symptoms are of diagnostic import, namely, (1) general signs of internal hemorrhage, (2) an abdominal tumor and (3) the appearance of "pseudopneumonia of the new-born" with a high temperature and rapid respirations, which are not accompanied by any signs of pulmonic involvement as elicited by physical or roentgenographic examination. Suggested therapy consists of intravenous transfusion of blood, injections of dextrose and the administration of a potent suprarenal cortical extract.

JACOBSEN, Buffalo.

STUDIES IN PASSIVE TRANSFER: IV. RECTAL ABSORPTION OF THE ANTIGEN (EGG WHITE). F. S. SMYTH and M. STALLINGS, J. Allergy **3**:16 (Nov.) 1931.

One-tenth cubic centimeter of antiegg serum was injected intracutaneously into the flexure surface of the forearm of twenty infants from 3 to 7 days old. A

colonic flush was given after a lapse of forty-eight hours to allow for sensitization of the local area. Twenty cubic centimeters of antigen solution (15 cc. of egg white with 300 cc. of distilled water) was injected slowly into the colon. Erythema and wheal formation resulted in all cases in from twenty to sixty minutes. Barium sulphate was injected with the antigen, and roentgenograms were obtained in two patients showing that absorption had taken place in the colon. A hereditary allergic trend was ruled out in the patients, and they are to be followed to see if the early introduction of raw egg white will result in hypersensitiveness or in any permanent skin reactions.

HOYER, Cincinnati.

MULTIPLE FRACTURES OF THE NEW-BORN. C. JEANNIN, M. SUREAU and R. WEILL-SPIRE, Bull. Soc. d'obst. et de gynéc. **21**:31 (Jan.) 1932.

A case is reported of an infant of 3,100 Gm., normally delivered, who at birth had multiple fractures of the long bones, including the ribs and clavicles. The mother had suffered during her pregnancy from vomiting, which started early and persisted till delivery. Toward the fifth month she had slight albuminuria and marked phosphaturia. Fetal movements were not often felt; they were not perceived at all for two or three days before delivery.

As a result of the fractures, the limbs of the infant were shortened by overriding and angulation. Crepitus could be elicited between the ends of the broken bones. The skull appeared larger than normal and was almost entirely membranous, only the lower portions of the occipital, frontal and parietal bones showing ossification. The sclerotics were markedly blue. The results of physical examination were otherwise normal. The reaction to the Wassermann test was negative. There was no family history of a similar condition. Except for the fractures, the roentgenograms showed no abnormality of the bones or centers of ossification. No new fractures occurred after birth, and the bones healed normally. The skull gradually ossified. The child was treated with mercury rubs, ultraviolet light, vitamins, calcium phosphate and arsenic.

The authors believed that osteitis fibrosa cystica, hereditary syphilitic osteopathy, congenital rickets and osteopsathyrosis could be ruled out. They considered that the condition resembled periosteal dysplasia more than anything else, but that it seemed to be an intermediate form, between that condition and osteopsathyrosis. Such conditions have been designated as "osteogenesis imperfecta," a term the authors prefer to use for the case described.

GLASER, Rochester, N. Y.

BIRTH TRAUMA TO THE LIVER. WEGELIN, Schweiz. med. Wchnschr. **62**:242 (March 5) 1932.

Within the liver of a 7 day old child, a large subserous hematoma was found at autopsy. This had ruptured the capsule and had bled into the abdominal cavity. The infant was unusually large, and the injury must be ascribed to birth trauma.

WOLMAN, Chicago.

THE INFLUENCE OF FLUID SUPPLY ON NEW-BORN INFANTS. S. A. TEN BOKKEL HUININK, Nederl. tijdschr. v. geneesk. **75**:5374 (Oct. 31) 1931.

The author examined the urine of twenty-one new-born infants. He found that with sufficient fluid supply the excretion of protein and other deviations of the urine nearly disappeared. He discusses the influence of the fluid supply on other symptoms of the new-born, as jaundice and loss of weight.

VAN CREVELD, Amsterdam, Holland.

Acute Infections

ACUTE TRANSVERSE MYELITIS COMPLICATING MEASLES. F. G. MILLER and A. G. ROSS, Canad. M. A. J. **25**:709 (Dec.) 1931.

This is the report of a case of measles with an acute, transverse myelitis in a girl of 11 years of age. The lumbar pain developed about three days after the onset of the measles. Paresis of the lower limbs and inability to control the urethral and anal sphincters occurred on the fourth day, and on the sixth day definite paresis of the arms developed. Within two weeks the patient began to improve. Examination two years later showed no residuals except a slight impairment of gait.

MOORE, Omaha.

THE PREVENTION AND TREATMENT OF WHOOPING COUGH. J. C. S. BATTLEY, J. Michigan M. Soc. **30**:344 (May) 1931.

The author summarizes the dangerous feature of whooping cough, particularly when it occurs during infancy, and stresses the necessity for having the parent aware of its seriousness. He gives the persistent cough, the lymphocytosis and the cough-plate culture more importance than the whoop in making the diagnosis. After thorough consideration of the general and nutritional care, an impartial survey of drug therapy is given. He supports vaccination, but more as a preventive than a therapeutic measure. He does not particularly advocate roentgenotherapy. He reviews the French literature on the injection of convalescent or adult serum with some favor.

SMITH, Ann Arbor, Mich.

PRACTICAL PROBLEMS IN POLIOMYELITIS. J. E. GORDON, J. Michigan M. Soc. **30**:937 (Dec.) 1931.

Gordon discusses the diagnosis and management of poliomyelitis in its three stages, the systemic period, the period of meningeal irritation and the stage of paralysis. During the first period he advises rest in bed and does not consider lumbar puncture or convalescent serum indicated. He gives good evidence for the use of whole blood administered intramuscularly at this stage. In the second stage lumbar puncture is recommended and convalescent serum intraspinally as well as intravenously, with the intramuscular use of whole blood from adults if the serum is not obtainable. His treatment of the third stage is that commonly employed at present.

SMITH, Ann Arbor, Mich.

RESULTS WITH TOXOID AS AN IMMUNIZING AGENT. D. J. BARNES, J. Michigan M. Soc. **30**:949 (Dec.) 1931.

Barnes objects to the use of toxin-antitoxin in that it sensitizes to horse serum, it protects only 80 per cent of patients and, by its failure to produce immunity universally, it undermines public confidence in immunization. Two injections of toxoid were given, one week apart, to 202 children under 5 years of age with a positive reaction to the Schick test. After one month 77.7 per cent gave negative Schick reactions, after two months 94 per cent gave negative reactions and after six months 98.5 per cent gave negative reactions.

SMITH, Ann Arbor, Mich.

SUMMARY OF CERTAIN NOTIFIABLE DISEASES IN THE UNITED STATES, 1930. Pub. Health Rep. **47**:560 (March 4) 1932.

In forty-eight states having a total population of 123,191,519, there were 228,354 cases reported of chickenpox, 66,576 of diphtheria, 419,465 of measles, 174,221 of scarlet fever, 48,907 of smallpox and 166,914 of whooping cough. One hundred and twenty deaths occurred from chickenpox, 5,971 from diphtheria, 3,433 from measles, 2,215 from scarlet fever, 170 from smallpox and 5,455 from whooping cough.

SANFORD, Chicago.

SOME OBSERVATIONS ON THE IMMUNITY AND DISABILITY CAUSED BY VACCINIA. SHELDON F. DUDLEY and PERCIVAL M. MAY, J. Hyg. **32**:25 (Jan.) 1932.

The results of first vaccinations as well as of revaccinations on those who had their primary vaccination in infancy are reported for a group of boys between 11 and 13 years of age. Reactions were classified according to the time the inflammatory areola round the site of insertion reached its maximum. They were designated as immediate (maximum within three days), accelerated (maximum from the fourth to seventh day) or primary (maximum reaction later).

Usually the size and severity of the reaction varied inversely with its rate of development. The typical immediate or "immune" reaction, a small unbroken papule with an areola about 10 mm. in diameter, indicates immunity to vesicular vaccinia.

Among 329 successful second vaccinations performed twelve years after the primary or first vaccination in infancy which left obvious scars, 37 per cent were "immune." Only 9 per cent gave primary reactions, the remainder being accelerated. Immune reactions were about 2.5 times as frequent in boys with 2 or more scars as in those with 1. Immunity depends more on the number than on the total area of the old scars.

Among 102 boys who had never been vaccinated before, there were no "immune" reactions, 4 accelerated reactions and 98 primary takes. About 75 per cent of the morbidity or sickness due to vaccination was caused by the primary vaccinations. Those vaccinated by the old technic with 2 or 3 scarifications had a morbidity 2.7 times higher than those vaccinated by 1 insertion of the lymph by the "multiple pressure" method.

The frequency of immediate reactions depends on many variables, among which may be potency, dose, strain of virus, time elapsing between two vaccinations, number of revaccinations, age and skin sensitiveness of the subject, etc.

The authors agree with Leake and Thomas, who said: "Judging by the immunity reaction, the smallest scar indicates the best," provided the number of scars is held constant.

Because of the lessened morbidity from the single insertion technic, with a minimum of trauma, this method is recommended over that of the multiple insertion, even though the protection may not be as complete and lasting.

JANNEY, Milwaukee.

IMMUNISATION WITH INACTIVE VACCINE VIRUS. J. O. W. BLAND, J. Hyg. **32**:55 (Jan.) 1932.

The apparent increase in postvaccinal encephalitis following the use of active vaccinia virus for the prevention of smallpox warrants attempts to produce a satisfactory inactive vaccine to replace it. Comments are made on the results (not too successful) of other investigators who have attempted to prepare a satisfactory inactive vaccine by various methods. The effort seems justified because of the effectiveness of the use of killed vaccines in other diseases (the phenolized vaccine of Semple for rabies, the formaldehydized vaccine for foot and mouth disease [here heat-killed vaccine is ineffective], Hindle's phenolized and formaldehydized vaccine in yellow fever, etc.).

Experiments were carried out on rabbits, guinea-pigs and monkeys. Inactivating agents were phenol, formaldehyde and heat. Results from subcutaneous, intracutaneous and intravenous inoculations were compared. Some immunity was developed, but in the main the work was considered a failure. Guinea-pigs showed the highest protection. The route of inoculation was unimportant. The author suggests that due to the delicacy of the antigenic structure its qualities are also destroyed by the inactivating agent, but that it seems reasonable that a satisfactory preparation may be developed.

JANNEY, Milwaukee.

POSTVACCINAL ENCEPHALITIS. A. CURRAU, Arch. de pediat. d. Uruguay **2**:367 (Aug.) 1931.

The author reports three cases of this disorder occurring in children of the age of 3½, 4 and 5 years. The symptoms developed five and one-half, ten and eleven days after the vaccination. The symptoms consisted of high fever, cephalalgias, somnolence or complete loss of sensorium, generalized or localized convulsions, loss of sphincter action and diminution or loss of reflexes. In one of the cases, the symptoms resembled those of tuberculous meningitis. In this condition the cerebrospinal fluid is generally normal. The evolution of the condition is usually rapid. One case ended in recovery, the other two in death. In one case serum from an elder brother who had been vaccinated at the same time was administered, but without success.

SCHLUTZ, Chicago.

REPORT OF AN EPIDEMIC OF SCARLET FEVER IN THE PAVILION (PROF. LUIS MORQUIO) OF THE HOSPITAL PEREIRA ROSSELL, IN THE YEAR 1930. EUGENIA S. YANUZZI, Arch. de pediat. d. Uruguay **2**:374 (Aug.) 1931.

The author reports forty-nine cases of scarlet fever, twenty-eight in girls and twenty-one in boys between the ages of 2½ and 14 years. Three of the children died within the first thirty-six or forty-eight hours after their admission to the hospital. These cases were of the malignant hypertoxic form, including one case of noma and one of pneumococcic peritonitis.

The most frequent complications were: buboes (eleven cases), acute glomerular nephritis (eight cases), bilateral otitis media (seven cases) and diphtheritic angina (four cases). The complications were always accompanied by a recurrence of the temperature.

Desquamation was observed in all of the cases by the third and fifth weeks. In the three fatal cases, the eruption was of the hemorrhagic type.

SCHLUTZ, Chicago.

ENCEPHALITIS FOLLOWING VACCINATION. ALBERTO ECKSTEIN, Arch. de pediat. d. Uruguay **2**:417 (Sept.) 1931.

Encephalitis following the administration of vaccine begins with severe cephalalgia, vomiting and some diarrhea. Convulsions then ensue with spastic paralysis, considerable prostration and deep stupor. There is generally a marked hyperthermia. The cerebrospinal fluid is generally clear, has few cells and generally no cellular reactions. The normal incubation of the disease is from five to fourteen days. The condition has not been observed in children under 2 years of age. It is more common in those vaccinated for the first time. The mortality is about 33 per cent. Convalescent serum in doses of from 8 to 10 cc. has seemed to give favorable results. The anatomicopathologic alterations found were: enlargement, edema and hemorrhagic areas in the cerebrum or spinal cord. The picture was that of encephalitis with perivascular infiltration. The author believes that those who become ill with this disease have some degree of predisposition to it.

SCHLUTZ, Chicago.

A CASE OF SPONTANEOUSLY GENERALIZED VACCINE. MIGUEL A. JAUREGUY, Arch. de pediat. d. Uruguay **2**:437 (Sept.) 1931.

This condition occurred in a boy 9 years of age. On the ninth day after vaccination he presented discrete pustules, and on the eighteenth day after vaccination showed a generalized eruption of the blisters which all appeared at one time. There was considerable febrile reaction. The author is of the opinion that the virus of the vaccine entered the blood stream and in this way caused the generalized eruption of vaccine pustules. There was complete recovery.

SCHLUTZ, Chicago.

TWO CASES OF NERVOUS COMPLICATIONS FOLLOWING MEASLES. GRACIA SCAFFO DE CASES MELLO, Arch. de pediat. d. Uruguay **2**:445 (Sept.) 1931.

In one of the patients, a child 8 years of age, severe chorea developed as a sequel to an attack of measles. Complete recovery occurred after rest in bed and treatment for chorea.

The second child, 12 years of age, presented a state of prolonged delirium in the course of an attack of measles. The condition lasted for forty-eight hours and ended in complete recovery without any untoward sequela.

SCHLUTZ, Chicago.

A CASE OF DIPHTHERIA CONJUNCTIVITIS IN AN INFANT. CARLOS M. BERRO, Arch. de pediat. d. Uruguay **2**:541 (Nov.) 1931.

This condition occurred in a girl 14 days old, accompanied by pronounced edema of the lids, a mucopurulent secretion and the formation of a false membrane. Deep ulceration occurred over the right cornea. Diphtheria bacilli were found in the cultures. General treatment and local therapy with serum gave relief from the condition, but a corneal leukoma persisted. There was no diphtheria in the family and no known contact with a diphtheria carrier.

SCHLUTZ, Chicago.

POSTSCARLATINAL NEPHRITIS WITH UREMIC CONVULSIONS AND HEMIPLEGIA WITH PERSISTENT APHASIA. LUIS MORQUIO, Arch. de pediat. d. Uruguay **2**:586 (Dec.) 1931.

This interesting combination of complications occurred in a girl 8 years old. It developed in the third week of a moderately severe attack of scarlet fever. The convulsive seizures lasted for twenty-four hours and were followed by complete paralysis of the entire right side of the body. In spite of improvement in the general condition, the paralysis persisted, and the child showed complete aphasia. Contractures of the paralyzed extremities gradually developed.

The aphasia persisted for a month and a half after the development of the illness. Laryngeal diphtheria developed, and intubation had to be instituted. There was reappearance of the nephritis. The child eventually recovered from this complication, but the hemiplegia and the aphasia persisted. The use of antidiphtheritic serum caused no aggravation of the nephritic condition.

The author believes that the hemiplegia and aphasia were ascribable to an embolism and an acute encephalitis.

SCHLUTZ, Chicago.

AMBIGUITY OF BLEPHARITIS DIPHTHERITICA. FRIEDMAN, Deutsche med. Wchnschr. **57**:1542 (Sept. 4) 1931.

A child of 2½ years had exhibited a scrofulous inflammation of the lids for about two months. The mother gave a positive tuberculous history, but thorough examination of the child failed to reveal any evidence of tuberculosis. The margins of the lids, especially the upper lids, showed a picture of eczema, interrupted by greatly inflamed masses, which were moist. No membrane was present. The conjunctiva, nares and throat were normal. The temperature was also normal. A culture was reported negative after twenty-four hours, but was later positive for diphtheria bacillus. A maid at the patient's home had a mild, moist eczema involving the outer canthi of both eyes. She had been under treatment for about a year, with no benefit. A culture demonstrated diphtheria bacillus. Both patients were cured by serum therapy, the child after eight days and the maid after two weeks. The author thinks that the organism was of the alternated variety.

MAYER, Chicago. [ARCH. OPHTH.]

POSTVACCINAL ENCEPHALITIS IN CHILDREN. V. NIEDERWIESER, Jahrb. f. Kinderh. **133**:318 (Nov.) 1931.

The author calls attention to the recent marked increase in postvaccinal encephalitis in the Tyrol, and reports two cases. The cerebrospinal fluid was inoculated into the cornea of the rabbit; no reaction typical of vaccinia resulted. Niederwieser calls attention to the presence of Guarnieri-like bodies in the control animals.

CLAUSEN, Rochester, N. Y.

DYSENTERY AGGLUTININS IN CHILDHOOD. THEA KORTMANN, Jahrb. f. Kinderh. **133**:355 (Nov.) 1931.

Recently dysentery and paradysentery bacilli have been found less frequently in cases of infectious diarrhea than formerly. The agglutinins occurring naturally against Bacterium dysenteriae are not specific

CLAUSEN, Rochester, N. Y.

SOME OBSERVATIONS DURING THE EPIDEMIC OF POLIOMYELITIS IN ESSEN IN 1929. BOSSERT, Jahrb. f. Kinderh. **134**:79 (Dec.) 1931.

The author gives rather general reflections on fifty cases of poliomyelitis. Two children in one family were infected. In one child, after a remission of eight days, fatal ascending paralysis developed. Poliomyelitis has formerly attacked several members of a certain family. Within 10 days fever and vomiting developed in over half the children of an orphanage; some of the children had meningeal irritation, and three had definite paralysis. None of the attendants had any symptoms.

CLAUSEN, Rochester, N. Y.

MALIGNANT DIPHTHERIA AND ITS TREATMENT. ULRICH FRIEDEMANN, Kinderärztl. Praxis **2**:241 (June) 1931.

Malignant diphtheria is a highly toxic diphtheria and not, as some have contended, septic diphtheria due to a mixed infection. Fatal diphtheria has been on the increase in Germany since 1926. The author distinguishes two forms of malignant diphtheria, the edematous and hemorrhagic. The latter is almost uniformly fatal; in the former the prognosis is grave, but a few patients recover. Death is nearly always due to circulatory failure, either early in the first two weeks or late, even up to the seventh week. In many cases diphtheritic nephrosis develops. Postdiphtheritic paralysis is common, although varying with the genus epidemicus.

The symptomatic treatment of malignant diphtheria is directed toward strengthening the circulation. Heart stimulants are of doubtful value, and epinephrine hydrochloride and a solution of pituitary gland given internally afford but temporary help. Intravenous thyroxine offers greater possibilities. Warm baths are strongly recommended. Fluid given subcutaneously or intravenously is often indicated.

The specific treatment is the more important. Friedemann, who has treated 10,000 patients with diphtheria, gives relatively large doses of antitoxin. He gives 4,000 units in mild cases, 10,000 units in moderately severe cases and from 20,000 to 150,000 units in severe and malignant cases. The larger doses are divided, not more than 50,000 units being given on the first day. In the severe cases the method of choice is the intravenous route, even though this involves certain dangers. Great care must be exercised to eliminate serum-sensitive persons (a careful history should be taken and preliminary small trial doses of serum given). It is of even greater importance never to give intravenously any antitoxin that has been treated with phenol or cresol U. S. P. The author uses a special serum which he obtains from the Danish National Serum Institute in Copenhagen; this serum is treated with oxyquinolin sulphate and is so concentrated that 10 cc. contains 50,000 units.

HUENEKENS, Minneapolis.

PERTUSSIS IN INFANCY. FRIEDRICH WILDTGRUBE, Kinderärztl. Praxis **2**:300 (July) 1931.

The author reports 165 cases of pertussis in infants, with a morbidity of 19.4 per cent. In infants under 3 months of age the mortality was 34.4 per cent; in those from 3 months to 1 year, 15.8 per cent. In all the fatal cases the infants had pneumonia; of those having pneumonia on entrance to the hospital, two-thirds died; of those acquiring pneumonia in the hospital, one-third died. The prognosis was much better when the infants were brought to the hospital early (mortality, 4.7 per cent). The treatment consisted of highly individualized care, small wards (never over five beds to a room) and fresh air. Vaccine therapy had no effect, but was given only in the convulsive stage.

HUENEKENS, Minneapolis.

THE DIAGNOSIS OF GONORRHEA IN CHILDREN IN PRIVATE PRACTICE. WILFRED COHN-HÜLSE, Kinderärztl. Praxis **2**:389 (Sept.) 1931.

The author is convinced that a diagnosis of gonorrhea in children is frequently made on insufficient evidence. Aside from a few cases of acute vulvovaginitis, in which the secretion contains practically no other organisms than gram-negative diplococci, the present state of our knowledge does not warrant a definite diagnosis of gonorrhea in children. The presence of a few gram-negative, intracellular diplococci is not sufficient to justify a diagnosis of gonorrhea. The author quotes statistics to show how, in such cases, several laboratories may differ in their bacteriologic diagnosis. In order to avoid the stigma of gonorrhea, with its sociological and psychologic consequences, these doubtful cases should be treated as gonorrhea but not diagnosed as such.

HUENEKENS, Minneapolis.

THE BACTERIOLOGIC DIAGNOSIS OF GONORRHEA IN THE CHILD. FRITZ VON GUTFELD, Kinderärztl. Praxis **2**:394 (Sept.) 1931.

The bacteriologic diagnosis of gonorrhea is made by means of the microscope and by culture. If large numbers of gram-negative, intracellular Diplococci are found in a smear from a vaginal secretion on two successive days, a positive diagnosis of gonorrhea may be made. If only a few such organisms are found, a positive diagnosis is justified only if such organisms are constantly present on repeated examinations and if a positive culture on a special culture medium can be obtained.

HUENEKENS, Minneapolis.

DIPHTHERIA AND DIPHTHERIA IMMUNITY. J. SIEGL, Med. Klin. **27**:1171 (Aug. 7) 1931.

This is an answer to the papers published by E. Friedberger in this journal. The author tries to refute the absolutely nihilistic attitude of Friedberger on the question of serum treatment of diphtheria and on diphtheria immunity. He admits that laboratory experiments cannot directly be applied to pathologic processes in human beings, but still maintains that the efficacy of antitoxin has been sufficiently proved. The failures of antitoxin are usually due to injection at a stage of the disease when it is too late. In such cases even high doses will fail to show any effect.

Passive immunization through injection of serum has also proved that the antitoxin content of the serum is the immunity factor.

The Schick test is considered as a true reaction of immunity. Friedberger's view that it is a change of reaction with age cannot be accepted. The author agrees with Friedberger concerning the value of active diphtheria immunization. Not all persons giving positive Schick reactions are susceptible to diphtheria, and a negative Schick test produced by active immunization does not mean that all persons are protected. The so-called negative phase has to be explained on the basis of decrease of antitoxin and not through a decrease of the general resistance of the organism.

ZENTAY, St. Louis.

MALARIA THERAPY AS A CAUSE OF CONGENITAL MALARIA. H. SCHADOW, München. med. Wchnschr. **78**:947 (June 5) 1931.

Schadow reports the case of a new-born infant admitted to the hospital for treatment for congenital syphilis. The mother had dementia paralytica, and the Wassermann reaction of the blood from the umbilical cord was positive. The infant was given potassium iodide. For two weeks the child was apparently well. During the third week a temperature ranging from 102 to 104 F. developed, and the spleen became palpable. In a few days regularity in the occurrence of the fever was observed. Examination of the blood revealed severe anemia and the tertian type of malaria plasmodia. It was then learned that the mother had received malaria therapy three weeks before her delivery. After six chills she gave birth to a premature infant weighing 2,300 Gm. The placenta was grossly normal.

The infant at first lost weight and was very sick. Treatment consisted of two blood transfusions and quinine hydrochloride, 0.025 Gm. twice daily, for twelve weeks with short intercurrent rest periods. The child's general condition improved rapidly. At the age of 7 months it weighed 7,200 Gm. At the age of 1 year there was no evidence of syphilis or malaria except a barely palpable spleen.

BRAHDY, Mount Vernon, N. Y.

SCARLET FEVER PROPHYLAXIS. BRÜGGER, München. med. Wchnschr. **78**:1082 (June 26) 1931.

Brügger used both active and passive immunization against scarlet fever to control an epidemic in an institution for children. The first injection for active immunization was given at the same time as the serum for the passive immunization. Two subsequent injections for active immunization were given at weekly intervals. Thirty-five cases with increasing frequency and severity had occurred in ten weeks preceding the beginning of immunization. Two hundred and twenty children and fifteen adults were immunized. Frequent local and general reactions were observed. One mild case of scarlet fever occurred fourteen days after immunization. Three other mild cases occurred during the next three months. Although the epidemic was checked, a change from a positive to a negative reaction to the Dick test occurred in only 61 per cent. To control an epidemic, Brügger advises that all persons in an institution who give a positive reaction to the Dick test should be subjected to both active and passive immunization.

BRAHDY, Mount Vernon, N. Y.

THE TREATMENT OF SCARLET FEVER WITH SERUM AND TRANSFUSION OF BLOOD. W. SCHULTZ, München. med. Wchnschr. **78**:1084 (June 26) 1931.

Schultz supplements serotherapy in scarlet fever with the transfusion of blood or the administration of convalescent serum. Donors for transfusion are used only if they show a negative reaction to the Dick test or if their serum produces blanching of a scarlet fever rash. Schultz thinks that the antiscarlatinal horse serum is not polyvalent enough and may not contain the one strain of streptococcus antitoxin necessary for a particular patient. In addition, nonspecific substances are made available to the patient by transfusion of blood or the administration of convalescent serum.

BRAHDY, Mount Vernon, N. Y.

THE RESULTS OF DIPHTHERIA PROPHYLAXIS IN MUNICH. M. PFAUNDLER, München. med. Wchnschr. **78**:1207 (July 17) 1931.

Pfaundler compared the morbidity and mortality from diphtheria among the children immunized during a period of seven years and those not immunized. Immunization was performed between the ages of 2 and 6 years by giving two injections of toxin-antitoxin from eight to ten days apart. Among the 2,485

children immunized, 18 cases of diphtheria developed. The incidence among the untreated children was four times as great. Whether the mortality rate was reduced could not be stated from these statistics, because none of the immunized children died, and in the untreated group 1 child died among 24 who contracted diphtheria.

BRAHDY, Mount Vernon, N. Y.

VARIATIONS IN THE CHARACTER OF DIPHTHERIA AND THE QUESTION OF MIXED INFECTION. R. HOPMANN and A. PANHUYSEN, München. med. Wchnschr. **78**:1208 (July 17) 1931.

The authors discuss the variations in the character of the diphtheria epidemics in different years. Not only the morbidity but also the mortality rate varies. Many investigators believe that the occurrence of severe toxic cases is due to a mixed infection, usually with streptococci. In some cases streptococci have been found in the blood stream. However, the complications that occur in the toxic cases are not the result of streptococcemia, but rather the toxic effects from diphtheria bacilli. Moreover, treatment of these cases with combined streptococcus and diphtheria serums did not decrease the mortality. The authors believe that the toxicity depends on the localization of the primary lesion. The localization varies in different years. Recently, the incidence of laryngeal diphtheria has been greatly decreased. If there is an increase in faucial diphtheria the number of toxic cases will increase. The basement membrane of the columnar epithelial lining of the larynx seems to inhibit the spread of the diphtheria bacilli, whereas this is not the case in the pharynx. Streptococci play an indirect rôle in the occurrence of toxic cases. An infection of the tonsils or pharynx by streptococci predisposes these tissues to infection by diphtheria bacilli. The more frequent the localization of the diphtheria bacilli in the oropharynx, the greater the incidence of toxic cases.

BRAHDY, Mount Vernon, N. Y.

TOXIC DIPHTHERIA. J. HUSLER, München. med. Wchnschr. **78**:1247 (July 24) 1931.

The increase in the severity of diphtheria has caused great concern to physicians. It is unfortunate that some investigators belittle the value of serotherapy. This has a harmful effect on the attitude of the practicing physician toward serotherapy. He may hesitate to give serum, which he is now told is not of such great value, until he is certain of the diagnosis. Husler reviewed sixty recent cases of toxic diphtheria, and found that in 63 per cent the physician had delayed one or more days before giving serum. Serum should be given during the first twenty-four hours of the illness. If this is done and a severe case develops, it is not necessarily due to failure of the serum. A particularly virulent organism may require serotherapy within eight hours to keep it under control. Husler urges the early and adequate administration of serum in all cases. He advises a maximum dose of 40,000 units given intramuscularly and intravenously. In conclusion, he suggests more extensive use of active immunization against diphtheria.

BRAHDY, Mount Vernon, N. Y.

DIPHTHERIA IN THE UNIVERSITY CHILDREN'S HOSPITAL FROM 1915 TO 1930, AND ITS THERAPY. H. SCHABER, München. med. Wchnschr. **78**:1249 (July 24) 1931.

This is another address before the Pediatric Society of Munich, dealing with the increasing severity of the cases of diphtheria in the Children's Hospital. Statistics show that there has been an increase in the morbidity and mortality of diphtheria in the last few years. Once an overwhelming toxemia has developed, there is little that can be done to help the patient. Administration of a combination of other serums with the diphtheria serum has not proved beneficial. Schaber urges adequate and early treatment with diphtheria serum.

BRAHDY, Mount Vernon, N. Y.

BLANCHING PHENOMENON IN POSTSCARLATINAL DERMATOSIS. W. SCHULTZ and R. BOVERI, München. med. Wchnschr. **78**:1487 (Aug. 28) 1931.

A boy, aged 7 years, was admitted to the hospital on the first day of his illness, with a mild attack of scarlet fever. A positive blanching test was obtained. On the fifth day of the illness, an eczematoid dermatosis with many small papules and vesicles developed. At the site of the original blanching test, which had not been especially distinct, there was now a definite area of blanching which stood out strikingly in contrast to the surrounding skin. A second blanching test done at this time was negative.

The authors state that this indicates a biologic relation between the secondary dermatosis and the scarlatinal streptococcus toxin. The exanthem was not due to a relapse, because it appeared too early and the second blanching test was negative.

BRAHDY, Mount Vernon, N. Y.

REVIEW OF THE FOREIGN CONTRIBUTIONS TO THE EARLY DIAGNOSIS OF ANTERIOR POLIOMYELITIS AND ITS TREATMENT WITH CONVALESCENT SERUM. W. MENK, München. med. Wchnschr. **78**:1521 (Sept. 4) 1931.

Menk reviews the results that have been published on the use of convalescent serum in the treatment of poliomyelitis. The majority of writers found that convalescent serum administered in the preparalytic stage reduced the incidence as well as the severity of the paralysis. The earlier in the preparalytic stage the serum was given, the more striking the results. Menk finds that the published reports would lead one to expect that the serum treatment of poliomyelitis in the preparalytic stage will prevent nine tenths of the severe paralyses and deformities. However, the author observes that many of the beneficial results were recorded without comparison with a suitable control series.

BRAHDY, Mount Vernon, N. Y.

GLANDULAR FEVER. H. BECKER, München. med. Wchnschr. **78**:1594 (Sept. 18) 1931.

Becker has observed ten cases of glandular fever in a half year. The characteristic symptom complex consists of fever, generalized adenopathy, enlargement of the spleen and a typical picture of the blood. At the beginning there is usually an absolute leukopenia and a relative lymphocytosis. In two instances, angina developed at the beginning of the third week of the illness, and in another case an erythema developed on the fifteenth day. There was a rise in the leukocyte count when these complications occurred. The fever may last from one to four weeks. In the charts shown, the pulse was slow in relation to the temperature. The prognosis is good.

BRAHDY, Mount Vernon, N. Y.

GLANDULAR FEVER. F. PARKES WEBER and O. B. BODE, München. med. Wchnschr. **78**:1598 (Sept. 18) 1931.

The authors describe six cases of glandular fever, three of which are the typical acute type described by Becker in the previous article. The other cases differed in some respects from the typical syndrome. In one case there was no adenopathy or splenomegaly, but the diagnosis was made on the presence of fever, a slow pulse and a characteristic blood picture. Similar cases without adenopathy or splenomegaly have been described. Another patient complained of fever and abdominal pain for one week. The fever persisted for a few more days. There was no adenopathy or splenomegaly. The picture of the blood was typical of glandular fever. This case falls into the group with enlargement of the mesenteric lymph nodes previously described by Glanzmann.

The authors made an interesting observation in regard to the Wassermann reaction in three cases. In two the Wassermann reaction was positive in the first

and second weeks of the illness. In the third case the Wassermann reaction was negative but the Meinicke reaction was positive during the third week of the illness. All the reactions became negative from four to eight weeks after the onset of the illness.

BRAHDY, Mount Vernon, N. Y.

POSTVACCINIAL ENCEPHALITIS. A. ESSER, Virchows Arch. f. path. Anat. **278**:200, 1930.

Esser reports two cases of acute cerebral involvement following vaccination against smallpox in infants aged, respectively, 3½ and 1¾ years. Fever and cerebral symptoms developed on the sixth and seventh days following vaccination, which was a first vaccination in each case. In the older child the histologic changes were those usually found in postvaccinial encephalitis: localized myelin sheath degeneration leading to complete demyelinization, focal glial proliferation and perivascular lymphocytic infiltration. In the younger child perivascular infiltration was absent, and changes of the myelin sheaths were very slight. There was, however, marked diffuse reaction of the glia and ganglion cells, the latter exhibiting varying degrees of degeneration. Inoculation of material from the younger child into rabbits had negative results. Negative results in experiments on animals do not warrant the conclusion reached by some that the vaccine virus itself cannot be the cause of the cerebral damage that may follow vaccination. Esser believes that in spite of negative results in inoculation of experimental animals, the vaccine virus may be the cause of the encephalitis.

SCHULTZ, Chicago. [ARCH. PATH.]

Chronic Infections

LIVER MEAL IN THE TREATMENT OF AMYLOIDOSIS IN SURGICAL TUBERCULOSIS. B. H. WHITBECK, J. Bone & Joint Surg. **14**:85 (Jan.) 1932.

The author states that amyloidosis in surgical tuberculosis is comparatively rare. However, when it does occur it is almost always fatal. Powdered whole liver, 1 teaspoonful three times a day, was used in seven cases. Five of these showed no evidence, clinically, of lardaceous disease after an eighteen months' period of treatment. One child died fourteen months after beginning treatment, although regression of the amyloidosis was evident. The seventh child died too soon after starting treatment to show any effects.

RYAN, Vancouver, B. C.

PREVENTIVE VACCINATION AGAINST TUBERCULOSIS WITH B C G. A. CALMETTE, Proc. Roy. Soc. Med. **24**:1481 (Sept.) 1931.

Koch discovered that the majority of human beings are spontaneously vaccinated against tuberculosis during the first period of life by the absorption of a few bacilli in milk or other food or by penetration into the organism by way of the mucous membranes or even the skin. If these infections are not repeated in a sufficiently long time, specific immunity against further or even more abundant infection is established. This can be obtained only for a very short time by the injection of bacilli killed by heat. Behring's method of bovine vaccination was soon abandoned because it was found that vaccinated animals intermittently excreted bacilli, which being sometimes virulent for guinea-pigs could be dangerous for animals or man. Other experiments were performed in an effort to avoid this drawback, but they were in vain. To secure preventive vaccination with the least risk, it is absolutely necessary to obtain a strain of bacilli definitely incapable of causing progressive tuberculosis in animals and man, even in high doses. It should be inoffensive, too, for susceptible animals and birds, but it should have the same antigenic properties as virulent bacilli and be able to provoke antibody formation. The author describes the early experiments on young calves with carefully prepared suspensions of bacilli which were mixed with their food. The

method of obtaining fine emulsions of bacilli is described. It was found that it was easier to emulsify bacilli grown on potatoes cooked in ox bile, and this bacillus is today designated as B C G (Bacillus Calmette-Guérin). Three experiments were interrupted by the war, but the authors had obtained valuable information. They were able to demonstrate that young calves given injections of bile bacillus showed a resistance to natural or experimental infections which lasted twelve or eighteen months. They then established immunity against tuberculosis by impregnating immediately after birth the lymphatic system of the young animal with attenuated bacilli, which, having kept all their antigenic properties, were incapable of causing active tuberculosis. Intraperitoneal injections were then given to guinea-pigs; these were followed by nodules in the epiploon. The nodules persisted for several weeks without doing any harm to the animals and finally vanished by resorption. It was impossible to find a trace of them, even with the microscope, when the animals were killed several months after the injection. The authors then felt that they had obtained a real vaccine. They were asked by Dr. Weill Halle if anything could be done for an infant, born of a tuberculous mother who had died shortly after delivery, who was to be brought up by a tuberculous grandmother. Since its chances of survival were precarious, they felt it their duty to make a trial of the method already tried out on animals. The results were very satisfactory, and the child developed normally during the six months following the vaccination. During the next three years 317 infants, 67 of whom were born and brought up in tuberculous homes, were vaccinated. The doses of B C G ingested by these infants were fixed at 30 mg., divided into three portions of 10 mg. each. They were given at forty-eight hour intervals. The authors insisted on the vaccination taking place immediately after birth and by ingestion. (Their reasons were given in the article.) After three years' work the B C G was put at the disposal of foreign laboratories. One question is most important: Is it possible that the B C G, after having lived a certain time in the organism without being killed or eliminated, becomes capable of causing progressive tuberculous lesions? A large amount of research work has been devoted to the solution of this problem, and so far no one can doubt the innocuousness of B C G, which remains avirulent in the organism of the vaccinated animal in which it acts as an antigen. Infants should be vaccinated at birth and then again at 3, 7 and 15 years.

A few comparative figures are given in vaccinated children and in children not vaccinated in France and Roumania. Of 579 children vaccinated more than four years before, who had lived continuously in tuberculous families, not one had died. This proves that B C G is at least innocuous and protected them against bacillary infection during four consecutive years. Finally, nearly a million children have been vaccinated in the last seven years, the world over, without any established accident due to B C G, so that now even the most hesitant person may be reassured.

WILLIAMSON, New Orleans.

THE CULTURAL DEMONSTRATION OF TUBERCLE BACILLI IN THE BLOOD STREAM OF GUINEA-PIGS AND HUMAN BEINGS. FRIEDA ABT, Schweiz. med. Wchnschr. **61**:1083 (Nov. 7) 1931.

Blood from infected guinea-pigs and sanatorium patients was planted on Löwenstein's and Hohn's artificial mediums. Tubercle bacilli were grown from thirty of a group of fifty animals. The blood of four of twenty patients yielded organisms. Postmortem cultures of the blood were made on four patients who had died of tuberculosis; two were positive. Löwenstein's medium was more satisfactory than Hohn's. Control cultures were run, which omitted the preliminary treatment of the blood with 3 per cent acetic acid, or 3 per cent acetic acid followed by 15 per cent sulphuric acid, as recommended by Löwenstein. These controls yielded a substantially higher percentage of positive growths.

WOLMAN, Chicago.

THE DIAGNOSIS OF TUBERCULOSIS IN INFANCY. T. GUGLIELMINI, Prat. pediat. **9**:199 (May) 1931.

This article is a brief review of tuberculosis in infancy and includes a good bibliography of the Italian literature.

DOOLEY, Kent, Conn.

THE CUTANEOUS REACTION OF PIRQUET AND THE INTRADERMAL REACTION OF B. TRAMBUSTI. P. DE STEFANIS, Riv. di clin. pediat. **29**:865 (Oct.) 1931.

In comparative tests on 300 children of Alexandria 153 reacted positively to the Pirquet test and 162 positively to the Trambusti test. The author prefers the latter test, because it is more sensitive and more easily interpreted. The percentages of children giving a positive reaction to tuberculin in Alexandria and its neighborhood as found by the author are as follows: children under 2 years, 38; from 2 to 6 years, 47, and from 6 to 12 years, 61.

HIGGINS, Boston.

A CASE OF POTT'S DISEASE WITH A COLD MEDIASTINAL ABSCESS. A. PUGLISI and O. MAROTTOLI, Arch. argent. de pediat. **2**:223 (May) 1931.

The authors present a case of tuberculous spondylitis in the thoracic column in a boy 14 years of age, which presented a few unusual features: the absence of a gibbus, and a cold mediastinal abscess which did not manifest itself clinically but presented the characteristic roentgenologic picture. The authors present a detailed and complete discussion of the pathology, symptomatology and treatment of Pott's disease. As to treatment they conclude: 1. The present surgical treatment is not capable of replacing the classic orthopedic treatment of Pott's disease. 2. Vertebral synostosis, which constitutes the surgical treatment of Pott's disease, can be of value only in conjunction with the orthopedic treatment and should not be used in all cases. 3. The surgical treatment has its best application in cases in which the tuberculous process is confined to the lower thoracic and lumbar regions of the spine. Only in exceptional cases should it be used when the process is localized to the cervical and upper thoracic region. 4. It has also its best effect when used late, only as a mechanical means of immobilization of a diseased column, the lesions of which are already beginning to subside. 5. Its contraindications are progressively developing abscesses, especially in the presence of fistulas, and the presence of paraplegias when there is danger of medullary compression.

SCHLUTZ, Chicago.

CLINICAL AND ANATOMIC PATHOLOGY OF CONGENITAL TUBERCULOSIS. A. SCROGGIE and T. KAUSEL, Arch. hosp. de niños **2**:1 (March) 1931.

The authors report two cases of tuberculosis. In one of them the tuberculous infection was undoubtedly of placental origin; in the other, infection probably occurred from the ingestion of tuberculous amniotic fluid during parturition. Autopsy in the first case showed the lesions to be present only in the abdominal organs, none being found in the lungs. The authors believe this distribution of lesions to be characteristic of congenital tuberculosis. In the second infant acute abdominal symptoms developed one month after birth. The mother was affected with florid tuberculosis, and died seventeen days after the birth of this child. At autopsy all the tuberculous lesions were found in the intestinal tract and peritoneum and throughout all the abdominal organs.

SCHLUTZ, Chicago.

SYPHILIS OF THE CENTRAL NERVOUS SYSTEM IN THE YOUNG INFANT. PEDRO ARAYA, Arch. hosp. de niños **2**:28 (March) 1931.

Latent syphilitic meningitis is fairly frequent, and occurs in the form of a slight meningeal irritation. Clinically it is not easily demonstrated. It is observed in about 1.6 per cent of syphilitic infants. Syphilitic meningitis in the young infant is manifested clinically by intracranial hypertension due to an acute hydrocephalus and by the absence of all other classic clinical signs observed in the meningitides of the growing child.

SCHLUTZ, Chicago.

Internal Diseases

GASTROPHOTOGRAPHY: FIRST RESULTS. C. GARIN and P. BERNAY, Arch. d. mal. de l'app. digestif **21**:558 (May) 1931.

Dr. Heilpern of Vienna has invented an apparatus for taking photographs within the stomach. Eight stereoscopic views are taken on sixteen negatives simultaneously. The apparatus is composed of a metallic tube 12.5 mm. in diameter and 7 cm. long, affixed to the end of a flexible sound. The metallic cylinder consists of simple black chambers without optic properties other than minute orifices 0.05 mm. in diameter. The chambers are grouped two by two in order to give stereoscopic views, and are separate in two parts facing toward the surfaces of the stomach. There are four negatives, or two stereoscopic views, on each face. Between the two cameras is the source of light, made by a tungsten filament protected by a thick glass.

The patient must be fasting. Obstruction and retention must be ruled out previously by roentgenograms. The apparatus, protected by a rubber casing that is suitably tense and fastened at its ends by ligatures, is introduced into the stomach under fluoroscopic control. When the apparatus is in place, the rubber casing is inflated, thus assuring the apparatus' being centered and distending the stomach; then the contact mechanism is brought into action. This has the effect of cutting the superior ligament and releasing the rubber casing. The tungsten filament is then short-circuited on the previously charged condensers, thus volatilizing the filament and giving a dazzling light easily visible through the abdominal wall. The films must be enlarged.

The whole procedure can be carried out in thirty seconds and is well tolerated, so that repeated examinations may be made without distress to the patient.

Several pages of illustrative reproductions of gastrophotographs are included in the article.

The authors do not state how fogging of the film is prevented while the camera is being introduced into the stomach under fluoroscopic control.

TURNER, Chicago.

THE THERAPY OF SEPSIS, MENINGITIS AND EMPYEMA BY ARTIFICIAL FORMATION OF ABSCESS. JACOB, Deutsche med. Wchnschr. **58**:48 (Jan. 8) 1932.

The author reports forty cases of sepsis, purulent meningitis, empyema, endocarditis lenta, and other conditions treated by artificial formation of abscess. In order to produce the abscess, from 0.75 to 2 cc. of turpentine was injected subcutaneously from one to three times. Twenty-nine patients recovered, in five the condition remained unchanged, and six died. After the injection of turpentine, fever, leukocytosis and a shift of the blood picture to the left occur, lasting for a few days. Then the fever falls to normal, the abscess breaks down or has to be opened, and the patient starts to recover. Jacob thinks that abscess therapy, though old, has never been fully appreciated. He feels that it is especially indicated in sepsis and other pyogenic diseases. Abscess therapy is not a specific treatment; its effect is based on leukocytosis, increased phagocytosis, production of specific antibodies, increased oxidation, increased permeability of the capillaries and excessive transfer of cell proteins into the blood stream.

KERESZTURI, New York.

OSSIFICATION OF THE SKELETON OF THE HAND: III. PHYSIOLOGIC OSTEOPOROSIS; IV. PATHOLOGIC OSTEOPOROSIS. E. STETTNER, Ztschr. f. Kinderh. **52**:1 and 14, 1931.

III. Osteoporosis of young children is due to physiologic changes occurring in the osseous system as a result of "Umbau," i. e., destruction and rebuilding. It occurs most frequently in the second year of life. It may be due to endogenous factors, but such exogenous factors as growth, nutrition and rickets contribute to the causation of this type of osteoporosis.

IV. Pathologic osteoporosis is due to hereditary factors or intercurrent infections which secondarily predispose to soft bones. Climate, together with other influences, may produce osteoporosis in young children. Osteoporosis sometimes results from the prolonged use of thyroid preparations. Cases are cited to illustrate pathologic osteoporosis.

SHELLING, Baltimore.

CONGENITAL CIRCULATORY DISTURBANCES. L. DOXIADES, Ztschr. f. Kinderh. **52**:141, 1931.

A case of congenital paroxysmal tachycardia is described. The tachycardia was of the auricular type, started on the seventh day of life and lasted for nine days. Three shorter attacks occurred in the following two weeks. The child has been well for the past twenty months, and no congenital defect of the heart or of the nervous system was found to account for the tachycardia. The author thinks that children born with unstable vegetative nervous systems are susceptible to such cardiac irregularities. He describes the syndrome and cites several cases. Two of these patients died suddenly without any apparent cause. At autopsy, enlarged thymi were found.

SHELLING, Baltimore.

THE THERAPY OF WERLHOF'S DISEASE. S. WOLFF, Ztschr. f. Kinderh. **52**:156, 1931.

Treatment of a severe case of purpura is described. The patient, a boy of 7 years, bled from the nose, vomited and coughed blood, and his entire body was covered with hemorrhagic spots. There was 15 per cent hemoglobin, and the red cells numbered 1,050,000. Transfusions were given several times, and the Gerson vitamin-mineral diet, calcium gluconate, an arsenic-liver preparation and a Spanish patent medicine said to contain all necessary vitamins were administered. The patient improved on this regimen and required only occasional transfusions. A second attack of bleeding was relatively mild, the hemoglobin falling only to 64 per cent. He is continuing on this form of therapy and receives a transfusion of blood once a month.

SHELLING, Baltimore.

BLOOD SUGAR IN NORMAL AND SICK CHILDREN, WITH SPECIAL REFERENCE TO CELIAC DISEASE. ELISABETH SVENSGAARD, Acta pædiat. (supp. 4) **12**:1 (July) 1931.

This is a monograph of 244 pages. The author used the Hagedorn-Jensen method, taking 0.1 cc. of blood at each determination and in the majority of instances making observations every five or ten minutes. Preliminary studies were carried out on fasting children. In the age group from 4 to 14 days, the average blood sugar value after a five-hour fast is 0.083 per cent; in the group from 15 days to 1 year, with a fasting period of from six to six and one-half hours, the average fasting value is 0.080 per cent. Children from 1 to 13 years of age fasting for from fourteen to fifteen hours showed an average value of 0.088 per cent. A few studies carried out during a prolongation of the fasting time described showed in some instances a tendency for the blood sugar to vary in long waves over a range of about 0.015 per cent, with a cycle of about eighty minutes, usually keeping within the normal limits for fasting values at the ages studied. Such waves may explain the different fasting values obtained on different occasions in the same individual.

The greater part of the work is taken up with tests for dextrose tolerance. In the youngest group, those from 4 to 14 days of age, the patients fasted for from five to five and one-half hours and 2 Gm. of dextrose per kilogram of body weight in a 10 per cent aqueous solution was then given. Determinations of blood sugar were made over a period of two and one-half hours. The examination was repeated after the interval of a few days. In one infant born at full term a flat curve at 8 days of age, followed by a normal curve with a peak

rise to 0.176 per cent at the end of seventy minutes, was obtained. Several infants showed hypoglycemic values at the end of the period of observation. In the test for dextrose tolerance, the general tendency of the curve for blood sugar to be flatter for infants in the first weeks of life than at a later age is independent of the trend of the weight curve at that time. In one premature infant there were rather flat curves both at 7 days and at 12 days of age.

In the group of infants from 15 days to 1 year, the dose of dextrose was also 2 Gm. per kilogram after a fast of from six to six and one-half hours. The shape of the curves was subject to greater variation for this age group than for any other studied, and one third of the children showed hypoglycemic values from two to two and one-half hours after the ingestion of dextrose. In a few nearly identical curves were found on two examinations made several days apart. In others, however, there was no resemblance of one curve to the other, and the second curve was not always lower than the first. Peak values of about 0.200 per cent were fairly common.

In the group from 1 to 13 years, the dose of dextrose was 1.5 Gm. per kilogram of body weight after a fast for from fourteen to fifteen hours. Less than one fifth of these children showed hypoglycemic values. In general there was a greater tendency for the curves of repeated tests to coincide at this age than in the case of the younger children. A statistical analysis of the results revealed little difference between the response of children from 1 to 13 years of age and that of adults, to this dosage of dextrose.

In a few infants under 1 year of age, the effect of different dosages of dextrose was investigated. In one case the amount was varied from 1 to 6 Gm. per kilogram; in another, from 2 to 10 Gm. per kilogram. There was no consistent relationship between dosage and the shape of the curve, nor between dosage and the height of the peak value. In a few tests in which the effect of sucrose was compared with that of dextrose, no striking differences were found.

Five children with celiac disease were examined. None of them showed an abnormal value for blood sugar during fasting. The majority showed little or no hyperglycemic rise after the oral ingestion of from 1.5 to 4 Gm. of dextrose per kilogram of body weight. This peculiarity persisted regardless of whether or not the patient's general condition was improving. Subcutaneous injections of epinephrine evoked a glycemic response in all subjects, proving that stores of glycogen were not depleted and that the dextrose-mobilizing mechanism was intact. When dextrose by mouth and hypodermic injections of epinephrine were both given, the curve rose higher and remained elevated longer. This was brought forward as evidence that the flat curve in the ordinary test is not based merely on failure of absorption of dextrose from the alimentary tract. One patient, given 1.5 Gm. of levulose per kilogram of body weight, showed again a flat curve, which was interpreted as evidence of normal function of the liver. The absence of hypoglycemia at any time during these tests is evidence that the flat curve shown by patients with celiac disease is not due to overproduction of insulin. No studies were attempted in which dextrose was given by a parenteral route. Control determinations were made on patients with chronic dyspepsia, with voluminous fatty stools; normal curves for blood sugar were obtained.

In four cretins, who showed low levels for blood sugar during fasting, the curves following the oral administration of from 1.5 to 2 Gm. of dextrose per kilogram of body weight tended to be rather low. In two of them treatment with thyroid produced a marked rise in the curve for blood sugar after the administration of dextrose.

In five infants with eczema there was a tendency toward high normal curves after the administration of dextrose. The author failed to confirm the results of Herlitz, who had found a definite dextrose tolerance in patients with eczema whose eruption was of less than two weeks' duration (abstr. in AM. J. DIS. CHILD. **36**:1042 [Nov.] 1928). In five infants with tetany accompanying rickets there was a tendency to low values during fasting, but otherwise normal curves for dextrose tolerance were found.

While special studies were not made to determine the threshold of renal excretion of dextrose, the evidence obtained in the course of these experiments indicated thresholds above 0.200 per cent.

McINTOSH, New York.

CHRISTIAN'S SYNDROME AND ITS RELATION TO GENERAL XANTHOMATOSIS. F. HENSCHEN, Acta pædiat. (supp. 6) **12**:1 (Dec.) 1931.

Two cases of xanthomatosis are reported; both occurred in children 3 years of age and in both autopsy was performed. Neither presented the complete Christian syndrome; one showed changes in the bones and exophthalmos but diabetes insipidus was not present; in the other there was no abnormal condition of the eyes. In addition, the author describes the histologic data on Kyrklund's case, already reported (*Ztschr. f. Kinderh.* **46**:56, 1926).

Two thirds of the article is devoted to a survey of the literature, with brief reports not only of all of the published cases of the full Christian syndrome but also of those showing xanthomatosis with any combination of one or two elements of the characteristic triad. There are also a few summaries of cases of xanthomatosis of the skin alone, generalized xanthomatosis alone and xanthomatosis associated with retardation of growth.

The conclusions reached in regard to the fundamental metabolic abnormality paraphrase those already expressed by Rowland in his classic article (Xanthomatosis and the Reticulo-Endothelial System, *Arch. Int. Med.* **42**:611 [Nov.] 1928).

McINTOSH, New York.

Nervous Diseases

SEX-LINKED INHERITANCE IN MENTAL DEFICIENCY. AARON J. ROSANOFF, Am. J. Psychiat. **11**:289 (Sept.) 1931.

After an analysis of data in ninety-five cases of mental deficiency in one or both members of pairs of twins, Rosanoff concludes that sex is an etiologic factor in feeblemindedness. He postulates that the genes of intelligence may be carried not only in the autosome, but also in the x-chromosome. In thirty-three of his thirty-five pairs of monozygotic twins, both members were mentally deficient; in only thirty-two of the sixty pairs of dizygotic twins were both members of each pair feebleminded. Two thirds of the feebleminded patients in his series were males. Of twenty-seven pairs of twins of opposite sex, there were sixteen in which only one member was deficient mentally; of these sixteen mentally deficient members, eleven were males. Rosanoff calls attention to the slight but consistent margin of superiority shown by girls over boys in scholastic records and intelligence tests.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

MENINGOCOCCIC (LATER ALSO STAPHYLOCOCCIC) MENINGITIS, LOW SPINAL SUBARACHNOID BLOCK, ABSCESS, LAMINECTOMY, RECOVERY. J. H. ARNETT, M. Clin. North America **13**:1051 (Jan.) 1930.

Only once before has a case of meningococcic meningitis followed by a staphylococcic infection been reported; this was by Osler in 1899. Arnett's case, therefore, is a rare one; although secondary infection of the meninges is not uncommon, it is generally due to the pneumococcus. In Arnett's case, the patient, a boy aged 14, had an attack of meningococcic meningitis with all the usual clinical and bacteriologic evidences of that disease. He seemed to be doing well following intensive treatment with serum until the eighth day, when the temperature began to rise again and he complained of generalized pains. At the same time, strabismus, optic neuritis and rigid retraction of the neck developed. On the eighteenth day, a combined tap was done, and both lumbar and cisternal fluids showed a growth of Staphylococcus aureus. Ten days later, evidence of block appeared — lumbar pressure could not be elevated by the Queckenstedt maneuver, whereas pressing

on the jugular vein caused a prompt rise in cisternal pressure. Objective examination and visceral symptoms localized the lesion at the second lumbar root of exit, and a laminectomy was performed. An abscess containing about 40 cc. of pus and a mass of matted cauda equina roots was found centrally in the dural sac at the level of the third lumbar vertebra. This was opened and drained, and the patient improved steadily, leaving the hospital on the twenty-seventh day after the operation almost entirely well.

Arnett considers that the optic neuritis in this case was not due to intracranial pressure but was rather a perineuritis of the optic tract representing an inclusion of the optic nerve meninges in the general meningitic process. Another unusual feature of this case was the appearance of the obstruction at the widest portion of the subarachnoid space, instead of, as is usual, at the narrowing due to the cervical or lumbar enlargements. Arnett advises keeping in mind the possibility of the formation of an abscess and block at the lowest portion of the subarachnoid space. A diagnosis must be made by comparative spinal manometry and careful neurologic study, and not merely on the basis of hyperesthesia and pain in the lower extremities. Because of the excellent outlook if the abscess can be localized and drained, recognition of this condition is of much practical importance.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

HELMINTHS AS A CAUSE OF MENINGITIS. L. J. M. LAURENT, Brit. J. Child. Dis. **28**:296 (Oct.-Dec.) 1931.

Night terrors, insomnia, general fidgetiness and movements that are vaguely choreiform have often been ascribed to the presence of intestinal worms. More serious nervous symptoms, e. g., generalized convulsions, temporary paralyses, loss of consciousness and a fully developed clinical syndrome of meningeal irritation, even with pathologic changes in the cerebrospinal fluid, have not been generally accepted as sometimes due to the same cause. A girl aged 3½ years was admitted with the story of having had several convulsions since the previous day. She had a temperature of 103.2 F., a pulse rate of 144 and a respiratory rate of 34. She was fretful and irritable and showed definite rigidity of the neck but negative Kernig and Brudzinski signs and no paralyses. Lumbar puncture showed a marked increase of pressure, but the spinal fluid was otherwise essentially normal. The following day and for four days thereafter under antihelminthic treatment the patient passed large numbers of thread worms. By the third day the patient appeared quite normal. The case was diagnosed as one of "helminthous meningismus." The various theories in reference to the cause of the meningismus are discussed.

LANGMANN, New York.

THE SIGNIFICANCE OF DETERMINING THE INTELLIGENCE FACTOR IN THE SPEECH DISORDERS OF CHILDHOOD. S. and M. BARTON HALL, Liverpool Med.-Chir. J. **39**:80, 1931.

Disorders in speech may be due to defects in the motor or sensory side of the speech mechanism or in the intellectual processes that are concerned in speech. The prognosis depends in a large measure on the level of the child's intelligence, and this should be determined in every case in order that time and energy may be spent where it is most valuable. Stammering depends on an inability to combine the laryngeally produced vowel sounds with the orally produced consonants, a defect of the motor mechanism which is heightened by a nervous factor. Lisping and lalling may be overcome in a normal child by simple procedures, but in a mentally retarded child little can be done. Idioglossia is primarily a defect of hearing, and as the child is unable to discriminate between sounds, the treatment depends on getting his confidence and interest and on careful practice in pronouncing and combining sounds and introducing them into short and then longer sentences. Congenital auditory imperception is a rare condition in which, though the sense of hearing is otherwise normal, there is a failure to appreciate the

significance of sounds. Worster-Drought and Allen have done the most work on this condition. In eighteen of fifty cases there was a familial factor. They suggest that the condition is due to a local bilateral aplasia of the cerebral cortex. The only chance of helping these patients is by cultivating the visual centers and using the eye as a means of teaching the child the art of lip reading and speech.

LESLIE, Evanston, Ill.

RIGID PROGRESSIVE SYNDROME WITH SPASM OF FORWARD TORSION. LUDO VAN BOGAERT and PAUL INGELBRECHT, J. de neurol. et de psychiat. **31**:118 (Feb.) 1931.

The authors report the case of a girl, aged 11 years, in whom dystonia with forward spasm and torsion had been developing for five years. This was followed by the development of difficulties in swallowing and later by a "progressive rigid syndrome," with generalization of voluntary motor activities and the association of athetoid movements and megasynkinesis. There was later found a weakness of downward gaze. These symptoms are suggestive of a condition described by Vogt as "status marmoratus," a case of which has been previously described by the authors. The authors do not believe that the condition could be explained on the basis of epidemic encephalitis.

WAGGONER, Ann Arbor, Mich. [ARCH. NEUROL. & PSYCHIAT.].

OBSERVATIONS AND EXPERIMENTS ON THE RÔLE OF INSTINCT IN THE CHILD. F. H. G. VAN LOON, J. de neurol. et de psychiat. **31**:309 (May) 1931.

The author defines instinct as a psychologic entity, which differs in its nature and manifestations from every other mechanism or psychic function, especially from intelligence, even if the constituents are absolutely the same. He states that instinctive functions in man are similar to those in animals. He concludes that the solution of each new problem by the child is associated with a certain degree of evolution, which concerns the relative intensity of instinct and intelligence. It is impossible to say at what stage infants first show evidence of intellect. At a more advanced age, they still lack understanding and intellect, because their capacities are not yet sufficient to repel satisfactorily their instinctive tendencies and mechanisms, or to vary them to fit their needs.

WAGGONER, Ann Arbor, Mich. [ARCH. NEUROL. & PSYCHIAT.].

ACUTE ENCEPHALITIC PARKINSONISM IN A CHILD FOLLOWED BY TORSION SPASM. A. KREINDLER, H. ELIAS and S. DIAMANT, Rev. neurol. **1**:486 (April) 1931.

In a boy 7 years of age parkinsonian symptoms developed on the fifth day of an illness accompanied by headache, somnolence and fever. There were rigidity and tremors, especially on the right. Nystagmus, trismus, incontinence and confusion appeared, followed by gradual improvement. It was noted that lymphocytosis persisted longer in the cisternal than in the spinal fluid. Four months later there was torsion spasm, turning the neck and trunk toward the right. There were tremors and contracture of the right arm and hand. The face was typically expressionless. The authors considered the case of interest because Parkinson's syndrome is not very common in children and because of its rapid development.

KISER, JR., Atlanta, Ga.

A CASE OF SYDENHAM'S CHOREA: ANATOMIC STUDY. PAUL VAN GEHUCHTEN, Rev. neurol. **1**:490 (April) 1931.

From anatomic studies, a double form of chorea has been suggested by Lhermitte and Pagniez, one form being inflammatory and the other degenerative. The author believes that this conception, as well as the diversity of opinion of other

workers, depends on the duration of the process in the particular case studied. When the disease has lasted a few days the inflammatory form is found, and when it has lasted from one to two months the degenerative form is found. He reports a study in a boy aged 15 years in whom typical chorea was present for fifteen days before death. The observations show a transition between the two forms. Degenerative lesions were found in the thalamus, caudate nucleus, putamen and certain areas in the cerebral cortex. These areas seemed to be the first injured, and the inflammatory process was subsiding. Similar but much less advanced degenerations were found in the dentate nuclei and Purkinje cells of the cerebellum. Evidence of fresh inflammation was found in the corpora quadrigemina, red nucleus and reticular formation. The toxic process thus had spread caudad from the basal ganglions. The primary and essential lesions in chorea are therefore in the thalamus, caudate nucleus, putamen and perhaps certain areas of the cerebral cortex.

KISER, JR., Atlanta, Ga.

BACILLUS ENTERITIDIS (GÄRTNER) MENINGITIS IN INFANCY. C. MALOSSI and F. ARA, Lattante **2**:581, 1931; reviewed in Prat. pediat. **9**:536 (Dec.) 1931.

After noting four previously described cases of Bacillus enteritidis meningitis, all fatal, the authors describe a case in a 6 month old baby who recovered. The spinal fluid showed a polymorphonuclear pleocytosis, organisms with the cultural and biologic characteristics of Bacillus enteritidis of Gärtner, albumin 0.20 mg. and dextrose 0.62 mg., but negative results in the Boveri, Nonne-Apelt and tryptophan tests. Therapy consisted in repeated lumbar and ventricular punctures, in numerous injections of autogenous vaccines and in roentgen irradiation of the head, this last treatment being given in the hope of preventing secondary hydrocephalus.

DOOLEY, Kent, Conn.

SYDENHAM'S CHOREA. ROBERTO INFANTE YÁVAR, Arch. hosp. de niños **2**:50 (March) 1931.

Rheumatism was associated with chorea in nearly all the author's cases. Endocarditis was not so frequently observed. No beneficial effect was observed from the use of neoarsphenamine. Solution of potassium arsenite was more effective in improving the symptoms of chorea, but did not shorten the course of the disease. The author has seen few cases completely cured in less than two and one-half months. Sodium salicylate is effective if rheumatism accompanies the chorea. Intramuscular autohemotherapy or intraspinal autoserum therapy was absolutely ineffective.

SCHLUTZ, Chicago.

PERMEABILITY OF THE HEMATO-ENCEPHALIC BARRIER FOR REST NITROGEN AND AMINO-ACIDS IN TOXIC STATES IN INFANTS. S. Y. SHAFERSTEIN, Jahrb. f. Kinderh. **132**:354 (Aug.) 1931.

In acute nutritional upsets, the author made the following observations (expressed in milligrams per hundred cubic centimeters):

		Nonprotein Nitrogen			Amino-Nitrogen		
	No. Cases	Blood	Cerebrospinal Fluid	Cerebrospinal Fluid/Blood	Blood	Cerebrospinal Fluid	Cerebrospinal Fluid/Blood
No intoxication.....	20	30-40	20-30	0.31-0.80	4.6-9.7	1.5-2.0	0.17-0.40
Intoxication.....	51	50-90	20-40	.....	4-9	1.2-5.6	0.15-0.96

No correlation was observed between the symptoms and the elevation of nonprotein nitrogen or of amino-nitrogen. In toxic states, the ratio of amino-nitrogen in the cerebrospinal fluid and in the blood may be raised; this is taken to mean increased permeability.

CLAUSEN, Rochester, N. Y.

Diseases of the Eye

GUNSHOT WOUND OF THE OPTIC NERVE. HALLIE HARTGRAVES and PETER KRONFELD, Arch. Ophth. **6**:554 (Oct.) 1931.

A 7 year old boy was shot in the head, the bullet entering 3 cm. in front of, and 5 cm. above, the right external auditory meatus. The right optic, oculomotor, trochlear and ophthalmic divisions of the trigeminal were involved. The ptosis disappeared; the movement of the right eye became normal, and the right optic nerve showed complete atrophy. The right pupil did not react to light, and the eye was blind. The authors consider this a case of amaurotic fixation of the right pupil.

WESCOTT, Chicago.

BUPHTHALMOS SECONDARY TO CONGENITAL IRIDOCYCLITIS. W. G. M. BYERS, Arch. Ophth. **6**:572 (Oct.) 1931.

This is a pathologic report of a case of buphthalmos secondary to congenital iridocyclitis. The condition was present at birth, and the author feels that this is a case of buphthalmos secondary to prenatal iritis and not a developmental aberration.

WESCOTT, Chicago.

A CASE OF ACUTE OPTIC NEUROMYELITIS. H. GRENET and TRIAU, Bull. Soc. de pédiat. de Paris **29**:388 (July) 1931.

A girl, 6 years of age, was admitted to the hospital because of sudden loss of sight. There was a mild papillary edema. She had incontinence of urine as well as paraplegia, and incontinence of feces soon developed. A rapidly progressing ascending paralysis with signs of bulbar involvement ensued, and the child died after a period of coma. Her stay in the hospital lasted sixteen days. She had fever during the illness, and it is thought that some infectious agent was responsible for the optic neuritis and the ascending myelitis. The spinal fluid was normal. Necropsy was not permitted.

BENJAMIN, Montreal, Canada.

HIGH MYOPIA IN THE FIRST YEARS OF LIFE: REPORT OF SEVENTEEN CASES. M. BARTELS, Klin. Monatsbl. f. Augenh. **86**:770 (June) 1931.

The term high myopia depends on the number of diopters and the age of the myopic person. Myopia of 3 diopters is considered high in a child, aged 3, but not in an adult. Bartels reports seventeen cases of congenital myopia, ranging from 7 to 23 diopters, in children, aged from 2 to 9 years; one case with myopia of 14 diopters in one eye and emmetropia in the other is included. The majority of the cases had changes in the fundus, e. g., conus, staphyloma, accumulation of rarefaction of the pigment and atrophy of the choroid. Nystagmus was present in three cases, divergent and convergent strabismus in three each and coloboma of the iris and choroid in one case. In some of these children disturbances in the growth of the body or retarded size was noticed, occasionally coupled with unusual mental development. Four cases showed progressive myopia, as far as could be ascertained.

The treatment depends on the etiology of the high myopia. Bartels, rejecting Donders' terms of destructive and nondestructive myopia, prefers the division into two groups: the progressive myopia of adolescence and the pathologic congenital myopia of the first years of life, based on malformation. His seventeen cases belong to the latter group, hence the treatment has to consist chiefly in strengthening the body, and possibly in a hormonal therapy, analogous with the use of thyroid preparations in disturbances of the growth in cretins. It is futile to resort to atropine in these cases, which have hardly any power of accommodation. Pilocarpine should be avoided, or used with care. Bartels observed detachment of the retina in a case of high myopia immediately after instillation of one drop

of pilocarpine. Moderate use of the eyes, on the other hand, and proper correction with glasses are recommended. Puncture of the anterior chamber and anterior or posterior sclerotomy may be considered. The child should attend sight-saving schools.

Bartels found the condition hereditary in six of his cases. In none was it due to consanguinity.

STOLL, Cincinnati. [ARCH. OPHTH.]

Diseases of the Ear, Nose and Throat

RELATION OF THE NARROW PALATAL ARCH TO NASAL AND SINUS DISEASE. HARRY L. BAUM, J. Am. Dent. A. **18**:1743 (Sept.) 1931.

The author attempts to disprove the theory held by many, that narrow high palatal arches cause deflected septums and a narrow nasal space. He cites cases in which the aforementioned nasal conditions are present in patients with wide palatal arches. He therefore contends that widening the dental arch by orthodontic means would have little effect on the nasal abnormalities. Delayed eruption of an incisor tooth is the cause of deviated septums, while the width of the nasal floor is dependent on the development of the antrums.

MARKUS, Philadelphia.

TOXINS OF STREPTOCOCCUS EPIDEMICUS FROM EPIDEMIC SORE THROAT. ISADORE E. PILOT and IRVING DREYER, J. Infect. Dis. **49**:135 (Aug.) 1931.

These authors describe a toxin due to Streptococcus epidemicus which they believe is different from the scarlet fever and erysipelas streptococcus toxins, as shown by skin testing and immunization experiments.

TOOMEY, Cleveland.

NEGLECT OF SLIGHT DEAFNESS IN CHILDREN. GEORGE B. MCAULIFFE, M. J. & Rec. **134**:29 (July 1) 1931.

The author points out that as soon as infancy is passed, children are allowed to go on an adult diet, without inquiry into their vitamin supply or the quality of their blood. No cod liver oil is given, and the children suffer from colds constantly. The children are not treated, as they do not seem ill, and are sent to school. They also suffer from anemia, constipation and poor digestion. All these conditions cause lowered resistance, and the children fall prey to catarrhal changes in the upper respiratory mucosa. These patients rarely have an audiometric examination unless they are really deaf. Slight impairments of audition go unnoticed. Children may never complain of earache or have an aural discharge and yet suffer from tubal catarrh and slight grades of otitis media. This state of affairs is so general between the ages of 7 and 14 years that the author feels impelled to make a plea for wider inspection of auditory acuity and nasopharyngeal catarrh. In all cases after whooping cough, measles, pneumonia or grip the patient should undergo an examination of his audition.

WILLIAMSON, New Orleans.

MASTOID INFECTIONS IN CHILDREN. B. M. KULLY, Nebraska State M. J. **16**:357 (Sept.) 1931.

The eustachian tube of the infant is shorter and straighter and has a larger lumen than that of the adult. The proximity of infected adenoid tissue, not only in the nasopharynx but throughout the lumen of the tube and even in the tympanic cavity itself, is another factor in mastoiditis. The tympanic membrane in early life is thicker and much more resistant to spontaneous perforation than in adulthood. This has a definite surgical bearing. The tympanic cavity of the child is of the same size as that of the adult. The mastoid antrum is relatively and absolutely larger. In general, acute otitis media is associated with acute mastoiditis. Mastoiditis demands surgical intervention under one or all of three conditions: (1)

extension of the infection through the mucous membrane with involvement of the osseous tissue and bone necrosis; (2) extension of the infection through the veins and possibly the lymphatics, with blood stream infection or threatened or actual intracranial complications, and (3) toxemia from continued absorption from the middle ear and mastoid foci. Acute mastoiditis is characterized by a sudden onset with acute symptoms unmistakably directed toward the middle ear and mastoid. Such cases, however, rarely require operation before the eighth day. Early mastoid tenderness, no matter how severe, is of no surgical significance. Tenderness that recurs, especially after the first week, is indicative of bone involvement and necrosis, and is an indication for operation. Elevation of temperature is usually present in children during the first few days of acute otitis and mastoiditis but, unless it is associated with chills, is of little importance. Persistence of or recurrence of fever after the first week, however, if other conditions, such as pyelitis or central pneumonia, are ruled out, is of surgical importance. Far more patients with mastoiditis are operated on too early than too late. Patients operated on early have the higher mortality. To operate before the body has mobilized its resistance, both local and general, increases complications. Recurrence of mastoid tenderness, especially if associated with swelling and edema of the mastoid process, indicates bone necrosis. Persistence of deafness into the second or third week is an important indication for operation. During the second week or later, operation in an uncomplicated mastoiditis is a relatively safe procedure. The operation should certainly not be performed on a presumptuous diagnosis, simply because gastro-enteritis is present. There must be definite findings in the otoscopic examination. Acute mastoiditis is to be regarded as associated with every case of acute otitis media.

HAMILTON, Omaha.

FOREIGN BODIES IN THE FOOD AND AIR PASSAGES. MURDOCK EQUEN, South. M. J. **24**:757 (Sept.) 1931.

There is no treatment for foreign bodies in the esophagus or tracheobronchial tree except early removal by means of endoscopy. Attempts at digital removal are wrong, as objects high up in the pharynx are frequently shoved down, into either the larynx or the esophagus. Slapping a child on his back or swinging him by his feet may cause violent inspiration to carry far down into the bronchial tree a foreign body that was originally high up, or the object may be caught by the vocal cords, causing sudden asphyxiation. When a history of swallowing or aspirating a foreign body is given, the patient should never be considered well until the foreign body is coughed up, removed endoscopically or passed in the stools. A history of the case is most important. This may elicit the occurrence of choking, gagging, cyanosis, wheezing respiration, pain, fever, cough, dyspnea, difficulty or pain in swallowing or regurgitation at the time of the accident. Roentgenograms should always be made, as they aid in the rapid localization of metallic objects.

SCHLUTZ, Chicago.

FOREIGN BODY IN THE TRACHEA. M. BOHÈME, Nourrisson **19**:185 (May) 1931.

An infant, aged 13 months, previously well, was brought to the hospital at Lunéville on account of marked dyspnea which had appeared suddenly. It was suspected that a foreign body had been aspirated. No bronchoscope being available, a tracheotomy was done. As the trachea was opened, a deep inspiration caused complete blockage. With the aid of a tracheal dilator and artificial respiration the patient was revived, and a fine forceps was introduced into the trachea. After several unsuccessful attempts, as the work had to be done blindly, the foreign body was grasped in the forceps and a large swollen bean extracted. The baby recovered.

MCCLELLAND, Cleveland.

BLOOD FIBRINOGEN IN TONSILLITIS. L. KOSTYÁL and S. FÉLEGYHÁZY, Arch. f. Kinderh. **92**:181 (Feb. 13) 1931.

Using the Van Slyke-Cullen method the authors examined the blood fibrinogen daily in thirty cases of uncomplicated tonsillitis and tonsillitis following scarlet fever and diphtheria. In the former there was an increase, particularly during the height of the fever. The same was true of scarlet fever and of uncomplicated diphtheria. In nephritis there was an early decrease in the first phase, followed by a strong increase. The fibrinogen was reduced in the uremic state. The authors explain this on the basis of blood colloids and capillary pressure, such as affects body fluids in edema.

SANFORD, Chicago.

THE GREAT TOE PHENOMENON AND GRÜNFELDER'S REFLEX IN OTITIS MEDIA AND IN INJURIES IN THE REGION OF THE POSTERIOR FOSSA OF THE SKULL. B. GRÜNFELDER, Ztschr. f. Kinderh. **51**:99 (May) 1931.

The Babinski reflex, on the one hand, and the great toe phenomenon and Grünfelder's reflex, on the other, are two different signs. The Babinski reflex is the expression of interrupted nerve paths; the great toe phenomenon and Grünfelder's reflex, the expression of increased irritability of normal paths. In the first six months of life, the difference between the two phenomena is this: The Babinski reflex is released by stroking of the sole; the great toe phenomenon occurs spontaneously or, as Grünfelder's reflex, is elicited by pressure on the skull. The Babinski reflex is fleeting, easily fatigued; the great toe phenomenon is lasting or, as Grünfelder's reflex, increases in intensity. At this age, even in the presence of the great toe phenomenon, a Babinski reflex can be obtained, but it is weak and can always be blotted out by the normal plantar flexion of the toes. If the Babinski reflex is present, as the result of damage to the pyramidal tracts, the other reflex cannot be obtained. The precipitation of blocking influences in the paths releases the Babinski reflex; a strengthening of the vestibular source of stimulation governing tonus releases the great toe phenomenon, a stimulation that is too weak in a normal baby, but goes over the threshold value in hemorrhages, inflammation or change of pressure in the posterior fossa or in the labyrinth. Grünfelder has studied these phenomena for three years in his wards in Jerusalem. Of 2,000 children, about 540 had a positive great toe phenomenon or Grünfelder's reflex. The usual cause was otitis media or mastoiditis, but it happened also with fracture of the base of the skull, a tumor at the cerebellopontile angle or a foreign body in the ear.

EMERSON, Boston.

CONSTITUTION AND SPEECH DISTURBANCES. T. S. FLATAU, Ztschr. f. Laryng., Rhin. (Teil 1: Folia oto-laryng.) **21**:63 (June) 1931.

Flatau points out that in a paper on the treatment for stuttering, which he read before the German society for voice and speech correction in 1928, he called attention to the fact that Jaensch's researches on the characteristic features of the physiology and pathology of the psychophysical personality, and especially the studies on capillaroscopy, have shown a way that will lead phoniatrics out of the stage of hypothesis toward exact comprehension of its psychophysical correlation. It is observed that children with speech disturbances often have one or several other defects, such as premature or retarded sexual development, infantile myxedema, an asthenic and eunuchoid habitus, hermaphrodism, dysthyreosis and other disturbances of the hormonal equilibrium, motor infantilism, hereditary syphilis, congenital debility, obstetric trauma, spasmophilia, paralysis, hydrocephalus, microcephalus, epilepsy, disturbances in affect, inhibitions, depressions, anxiety, phobias, hypersensitivity, fitfulness, excessive timidity and anomalies of walking, writing and facial expression. This concurrence of speech disturbances with other anomalies indicates the constitutional character. The author defines constitution

and further differentiates between two main groups of persons with speech defects, the neuropathic and the psychopathic; he then reports results of studies on patients with speech disturbances. The patients were subjected to cranial measurements, roentgenoscopy of the head, especially of the sella, electrical irritability tests, psychotechnic and psychologic examinations and capillaroscopy. The results of the capillaroscopy are described in detail, and several case reports are given. The author does not wish to overemphasize the significance of capillaroscopy; however, he found that it permits a clear diagnosis and careful observation during the course of treatment. He states that in most cases a combined phoniatric and lipoid therapy proved helpful. The latter was employed in the form of a lipoid iodine preparation. In cases of hypothyreosis or hypophyseal disorders the respective organ preparations were helpful, and calcium, iron, bromine, phenobarbital and vitamin preparations were likewise given if necessary. The phoniatric treatment consisted of proper speech exercises.

EDITOR'S ABSTRACT [ARCH. OTOLARYNG.].

HEMORRHAGE AFTER PERITONSILLAR ABSCESS. P. G. GERLINGS, Nederl. tijdschr. v. geneesk. **75**:2578 (May 16) 1931.

Three cases of severe hemorrhage after peritonsillar abscesses in children are reported; in two cases the hemorrhage caused the death of the patient. The explanation of this complication is given and the literature is considered. The author is of the opinion that in every case of severe or repeated hemorrhage after peritonsillar abscess, ligation of the common carotid artery is indicated; in exceptional cases ligation of the external carotid artery is sufficient.

VAN CREVELD, Amsterdam, Holland.

Diseases of the Skin

A STUDY OF THE STIMULATING EFFECT OF SMALL DOSES OF THALLIUM ACETATE ON THE RATE OF GROWTH OF HAIR IN THE ALBINO RAT. ZOLA K. COOPER and MARTIN F. ENGMAN, Arch. Dermat. & Syph. **23**:1031 (June) 1931.

The results obtained seem to justify the conclusion that small doses of thallium acetate produce some stimulation of the rate of growth of the hair. Doses of from 0.004 to 0.006 Gm. per kilogram of body weight produced an 18 per cent increase in the growth of hair. Smaller doses produced no change in growth. Doses of 0.008 Gm. per kilogram caused a falling of hair. The last-mentioned dosage has been used for some time in mycotic infections of the scalp.

HENNING, Iowa City.

TREATMENT OF ERYSIPELOID BY LOCAL INJECTIONS OF SPECIFIC SERUM: REPORT OF A CASE. EARL B. RITCHIE, Arch. Dermat. & Syph. **23**:1069 (June) 1931.

The author records a case of erysipeloid infection of the palmar surface of the hand that was cured with repeated local injections of Erysipelothrix suis (Mulford); 8 cc. was used in all. The bacillus of swine erysipelas was isolated.

HENNING, Iowa City.

ANGIOKERATOMA: COMPREHENSIVE STUDY OF THE LITERATURE AND REPORT OF A CASE. EUGENE F. TRAUB and JESSE A. TOLMACH, Arch. Dermat. & Syph. **24**:39 (July) 1931.

The author sifted the literature for the typical cases described by Mibelli in 1889, and listed them as "angiokeratoma Mibelli" and the atypical cases as angiokeratoma without pernio (Fordyce). The typical case is rare. The typical

lesions begin in early childhood, preceded by pernio and have a hereditary background. The lesions are rough, hard, warty elevations, from the size of a pinpoint to that of a pinhead and located on the hands, feet, knees and elbows. The relationship between angiokeratoma Mibelli and tuberculosis cannot be proved. The authors feel that the two conditions are not of the same nature.

HENNING, Iowa City.

BACTERIOPHAGE THERAPY FOR PYODERMIA. BARNARD L. KAHN, Arch. Dermat. & Syph. **24**:218 (Aug.) 1931.

The author reports twenty cases: nine of acne, five of furunculosis and one each of hordeolum, alveolar abscess, bed sore, sycosis vulgaris, ischiorectal abscess and ringworm of the toes with secondary infection. Staphylococcus bacteriophage was injected subcutaneously and applied over and in the exposed lesions of some of the patients. From 2 to 3 cc. of this bacteriophage was used at three day intervals, and in some cases a moderate anaphylactic reaction occurred. The cases were benefited from 50 to 90 per cent, and the author feels that this treatment is a worth-while contribution to the therapy of pyodermia.

HENNING, Iowa City.

SUBUNGUAL EXOSTOSES. LOREN W. SHAFFER, Arch. Dermat. & Syph. **24**:370 (Sept.) 1931.

Subungual exostosis develops more frequently during adolescence than at any other age. It is three times as common in women as in men, and may resemble an ingrowing nail, simple fibroma or, at times, a malignant condition. Trauma may be a cause, but this exostosis arises too constantly from the tibial side of the ungual phalanx of the great toe. It is a solitary, benign, slow growing, pea-sized, painful tumor, appearing as a fibrous nodule and readily diagnosed by roentgen examination except very early in its growth. It arises as a cartilaginous outgrowth and later becomes osseous. Complete surgical removal is the treatment of choice.

HENNING, Iowa City.

ACUTE DERMATITIS DUE TO OPIUM PREPARATIONS. N. B. HELLER, Arch. Dermat. & Syph. **24**:417 (Sept.) 1931.

The author reports a case of acute dermatitis that occurred in a boy, aged 6 years, owing to the use of opium preparations externally and internally. The observations were corroborated both by the patch test and by the results of experimental internal administration.

HENNING, Iowa City.

TREATMENT OF PSORIASIS: CONTINUED OBSERVATIONS ON THE USE OF CRUDE COAL TAR AND ULTRAVIOLET RAYS. WILLIAM H. GOECKERMAN, Arch. Dermat. & Syph. **24**:446 (Sept.) 1931.

The author has treated and observed many patients with psoriasis over a period of many years, and concludes that this treatment is one of the simplest, cheapest and most effective methods to control individual attacks. Arthritis associated with psoriasis is materially benefited also. The formula of the crude coal tar is as follows: crude coal tar, from 2 to 6 cc.; zinc oxide, 1 ounce (28.35 Gm.), and petrolatum to make 4 ounces (113.4 Gm.). An air-cooled quartz lamp is used, and the dosage is increased daily to skin tolerance. Mild conditions clear up in from two to three weeks, and severe conditions in from three to four weeks. The daily procedure is as follows: application of the ointment, followed the next day by irradiation with quartz light after most of the ointment is removed; a soap and water or a soda bath, and reapplication of the ointment from four to six hours later.

HENNING, Iowa City.

INFANTILE ECZEMA. F. S. SMYTH, K. M. BAIN and M. STALLINGS, J. A. M. A. **97**:1291 (Oct. 31) 1931.

A study of eczema, based on 160 cases, led the authors to conclude that it is a response to skin irritation the source of which may be multiple or single and related to local infection, to cold or heat or to intolerance of an allergic nature. Allergen frequency is not based entirely on contact but probably on some immunochemical mechanism. Skin reactions rarely develop before the fourth month, and may be lacking. In some instances allergy is only an additional factor. During treatment the diet must not be restricted so as to prevent normal nutrition.

BONAR, Salt Lake City.

FOLLICULITIS DECALVANS, KERATOSIS PILARIS AND ONYCHOGRYPHOSIS. J. GATÉ, P. CUILLERET and C. E. BOYER, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Lyon) **38**:1033 (July) 1931.

A girl, aged 8 years, had a disease of the scalp of two years' duration. A large oval area of cicatricial alopecia covered the occipital and parietal regions. The edges of this zone were erythematous and were occupied by numerous points of suppurating folliculitis, the hairs being easily extracted. Microscopic examination and culture of the hairs gave negative results for spores or mycelia. The eyebrows were gone, and the skin of the forehead and face showed erythema and marked dryness, with a fine desquamation. Characteristic lesions of keratosis pilaris occupied the nape of the neck and the extensors of the extremities. The finger-nails and toe-nails, especially the latter, exhibited a typical onychogryphosis. Several teeth showed dystrophic changes, the incisors particularly having suggestive though not definite, hutchinsonian characteristics. In spite of negative serologic tests, and no other clearcut clinical evidence of congenital syphilis, the presenters wondered whether, in view of the abnormalities of nails and teeth, the institution of antisyphilitic treatment might not be justified. The differential diagnosis between the scarring forms of alopecia was discussed, the decision being in favor of a diagnosis of folliculitis decalvans in this case.

GANDY, Houston, Texas [ARCH. DERMAT. & SYPH.].

STATISTICAL STUDY OF KELOIDS. NAEGELI, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Strasbourg) **38**:905 (July) 1931.

This paper is a statistical study of the frequency of keloids. In an examination of 3,335 healthy school children, the author found keloids in 151, an incidence of 4.5 per cent. Below 10 years of age the condition predominated in boys, while in children from 10 to 15 years the difference between the sexes was slight. The preponderance of these keloids existed in vaccination scars. The incidence was much higher in the later age group than in the earlier. Among 834 adults examined, 112, or 13.3 per cent, had keloids. In the aged they were rare. An entire hospital population of 530 patients suffering from various acute and chronic diseases, both children and adults, were also examined, and the incidence of keloids was found to be much higher than in the group of healthy persons. Among 49 patients with tuberculosis, 11 (22.4 per cent) had keloids.

GANDY, Houston, Texas [ARCH. DERMAT. & SYPH.].

LYMPHANGIECTASIS WITH CHYLORRHEA. NING, Dermat. Wchnschr. **93**:1389 (Sept. 5) 1931.

The patient first noted the condition at the age of 11 years, at which time a group of vesicles developed on the inner surface of the right thigh which discharged a white fluid at intervals of about fourteen days. The urine was milky at times, but cleared when the cutaneous lesions were discharging. The patient

was again admitted to the clinic at the age of 34. There was a considerable swelling of the right leg and thigh, which had been increasing for three years, and also a good deal of pain. The number of vesicles was increased, new groups having developed at the site of an incision of a furuncle on the hip. Chemically, the fluid proved to be chyle rather than lymph. Sections showed dilatation of the lymph vessels with vesicles in the epidermis. The etiology was apparently an abnormal connection between the chyle and lymph vessels in this region.

TAUSSIG, San Francisco [ARCH. DERMAT. & SYPH.].

MULTIPLE BENIGN SARCOID IN A BABY. R. POLLAND, Dermat. Ztschr. **61**:360 (Aug.) 1931.

A 5 month old baby was observed who had about fifteen small nodules scattered over the scalp, forehead, shoulders, arms, chest and inner malleolus of the left ankle. These were moderately hard and chocolate brown, with no tendency toward necrosis. The tuberculin reaction was negative. Biopsy showed pigment granules scattered through the epidermis and corium and round groups of oval and short spindle cells, but no giant or epithelioid cells. The condition cleared with little therapy and is considered by the author to have been multiple benign sarcoid.

TAUSSIG, San Francisco [ARCH. DERMAT. & SYPH.].

TREATMENT OF SCLERODERMA WITH PANCREAS. J. SELLEI, Orvosi hetil. **75**:13 (Jan. 3) 1931.

Raw pancreas, ground and mixed with soup or broth, was given daily. The amount for children ranged between 30 and 50 Gm. It was, as a rule, given from one to one and a half hours before breakfast. An hour later pepsin and hydrochloric acid were given in small doses. In the first stages of scleroderma, when there was no atrophy, good results were seen in from four to six months. No relapses were noted.

ZENTAY, St. Louis.

Surgery and Orthopedics

ACUTE SUPPURATIVE PAROTITIS: A PATHOLOGIC AND BIBLIOGRAPHIC STUDY WITH REPORT OF TWO CASES. R. P. CUSTER, Am. J. M. Sc. **182**:649 (Nov.) 1931.

Acute suppurative parotitis may occur as a complicating infection in a wide variety of conditions. It may take its origin through the duct or by the hematogenous route. Two cases are presented, both terminating fatally, which favor the theory of the ductogenous route, but there is evidence in favor of each view. In each of the aforementioned cases the histologic picture is given. A review of the literature on this subject from 1858 to date is presented.

HENSKE, Omaha.

INJURY TO EPIPHYSIS OF LOWER END OF ULNA AND RESULTING DEFORMITY: CASE REPORT. EDGAR BIRDSALL, Am. J. Roentgenol. **23**:208 (Feb.) 1930.

A boy, aged 15 years, was examined five years after an injury to his wrist. Roentgenograms revealed that the head of the ulna, epiphysis and lower end of the diaphysis were missing and that the radius was bowed, with the head pushed well up into the elbow joint. A fracture of the ulna in the region of the epiphysis was followed by absorption of the head and diaphysis, which resulted in an arrest of development of the lower end of the ulna. The radius continued to develop, with the resulting deformity.

STULIK, Chicago.

SYMPTOMS AND PHYSICAL SIGNS INDICATING HERNIA OF THE DIAPHRAGM WITH REPORT OF TWELVE CASES TREATED BY OPERATION. PHILEMON E. TRUESDALE, Ann. Surg. **94**:528 (Oct.) 1931.

The symptoms of hernia of the diaphragm are odd because of their variety and complexity, and the condition is therefore often undiagnosed. In adults the clinical picture bears such close resemblance to the symptoms of diseases of the heart, lungs, stomach, gallbladder and intestines that the deformity is not thought of. In infants cyanosis is an invariable accompaniment of congenital hernia of the diaphragm, and yet is seldom considered because it is so often a manifestation of an enlarged thymus and heart disease. The physical signs found are dependent on the amount of hollow abdominal viscera in the pleural cavity and vary according to the amount of food, water or air in the stomach and bowel. It is not uncommon to find different physical signs at each examination. In spite of the many vagaries, the herniated viscera show important signs. The affected side of the chest is prominent and restricted in motion. Outward flaring of the margin of the subcostal angle due to loss of pull by the diaphragm against the scalene and intercostal muscles is often observed. Litten's sign is absent. The abdomen may be scaphoid. Dextrocardia is always present in some degree in hernia on the left side. Most important in the examination is the roentgenogram. An opaque meal should be given to show the position of the stomach and the intestines; this should be followed by a barium sulphate enema to define the location of the colon.

The treatment depends on the form of hernia and the symptoms produced by it. Diaphragmatic hernia sometimes exists throughout life without causing symptoms, as has been demonstrated by postmortem examination. Bearing in mind the mechanical effects produced by the transposed hollow viscera and the tendency for peristalsis to be impeded, it is natural to infer that a reduction in the volume of gas would afford immediate relief. This may be accomplished, first, by placing the child in the upright posture and, later, if necessary, by passing a stomach or rectal tube. Regulation of the diet and antifermentatives may be used. If these measures fail, the author advises operation, but cautions that it invariably assumes major proportions, and may more easily be performed before the adolescent period. He gives a detailed and well illustrated description of the preoperative care and intrathoracic operation as performed by him. He emphasizes the importance of a complete physical examination, a careful inspection for other congenital defects, roentgen examination of the thymus and the utmost care in minimizing the wear and tear of exhaustive investigations. The anesthetic advised is pressure gas oxygen ether.

BANTIN, Omaha.

SELECTIVE SURGICAL TREATMENT OF DIAPHRAGMATIC HERNIA. CARL A. HEDBLOM, Ann. Surg. **94**:776 (Oct.) 1931.

Diaphragmatic hernia is a protrusion of the abdominal contents through an abnormal opening in the diaphragm, which results from imperfect development, anatomic weakness or trauma. Of 1,003 cases reported in the literature since 1900, nearly one third were classed as congenital, a little more than one third as acquired after birth and about one third as following trauma. In each of these anatomic types there are many anatomic and clinical variations which the author discusses. Age is an important factor in the consideration of treatment. In 210 nontraumatic cases in patients 1 year of age, death occurred in 75 per cent before the end of the first month after birth. Autopsy was performed in all of these cases. Since serious respiratory embarrassment is often associated with a hernia opening that is too large for direct closure, it follows that the chance of saving many of these infants is slight. The ideal surgical treatment is reduction and repair of the hernia opening. The repair may be accomplished through either a laparotomy or a thoracotomy exposure; occasionally both must be used. According to the figures usually cited, the mortality rate following laparotomy is much

higher than that following thoracotomy, but this difference seems to be due to the relatively much larger proportion of cases of obstruction in which a laparotomy is performed. A very high mortality rate follows the combined thoracotomy and laparotomy probably because of shock and an increased incidence of postoperative complications. A primary laparotomy is indicated in all cases of acute intestinal obstruction if there is a doubt as to its cause. Thoracotomy, on the other hand, is the only approach in cases of fresh penetrating wounds of the thorax with prolapse of the abdominal contents. The author discusses the limitations of both methods and special procedures for closure.

BANTIN, Omaha.

SPINA BIFIDA. W. T. COUGHLIN, Ann. Surg. **94**:982 (Dec.) 1931.

The successful repair of any serious congenital defect in the new-born usually carries with it its own reward, but in the case of spina bifida the author does not believe that this is true. The operations themselves are usually technically successful, but the after condition of the patients often does not justify the operation. The incidence of spina bifida is one in a thousand births. As yet the etiology is unknown.

The author discusses at length the types of spina bifida and the kinds of operations performed. If the little patients with spina bifida of the myelocele or myelocystocele variety are not operated on promptly, death is likely to occur. If the meningocele has a normal skin covering, the patients may grow to adult life. The presence of hydrocephalus or vesical or rectal paralysis is said to contraindicate operation. No one has reported a case wherein congenital paralysis of bowel or bladder was cured by operation for spina bifida.

Early operation is advised, before the third day of life, if possible, as babies of this age are not so susceptible to shock as older children.

Twelve case histories are given in detail.

BANTIN, Omaha.

APPENDICITIS IN INFANCY. BENJAMIN LIPSCHUTZ, Arch. Pediat. **48**:649 (Oct.) 1931.

Two cases of appendicitis occurring in infancy are reported in detail. The incidence and peculiarities of appendicitis at this age are discussed. The difficulties in diagnosis are pointed out, and the necessity of early operation is stressed.

WADDELL, University, Va.

CLEFT LIP AND PALATE: ITS SURGICAL CORRECTION. ALBERT D. DAVIS, California & West. Med. **35**:357 (Nov.) 1931.

According to the author the aim of operations on the palate should be the formation of a firm bony union of the maxillae and premaxillae and a perfect union of the soft tissues throughout. The latter should be long enough to close the postpharyngeal space, and flexible enough to control the amount of air passing through the oronasal communication so as to allow normal respiratory function. A long flexible palate, capable of perfect function and speech, is desired. When the bones are united first, a normal foundation for operations on the lip, nose and soft tissue is formed, there is more normal occlusion of teeth, with a resulting foundation for orthodontic treatment, and oronasal sinuses are prevented. Following the operation on the bones, closure of the lip should be effected. The operation of choice should be one that does not sacrifice lip tissue, that brings the nose into normal position and that gives normal shape and contour to both nose and lip. To be avoided are: (1) a sacrifice of too much tissue, (2) making the lip too long, (3) a lack of central fulness, (4) notches in the lip, (5) scar tissue, (6) tension and (7) infection. The technic of the operations is described in some detail.

DICKEY, San Francisco.

LAMINECTOMY IN SPINAL INJURIES. EDGAR F. FINCHER, JR., J. M. A. Georgia **21**:62 (Feb.) 1932.

Laminectomy is performed to relieve pressure on the spinal cord; the pressure is usually caused by bony fragments. Laminectomy is indicated, therefore, when there is a possibility of restoration of function. In evaluating the degree of damage, a careful neurologic examination is essential. Roentgenograms should be made in three planes. Spinal puncture should be performed to reveal possible hemorrhage and to test the patency of the canal by the method of Queckenstedt.

The following is an illustrative case: A colored child was seen two hours after injury to the back. There were motor changes of the right knee and of the left leg. Sensation to light touch below the first lumbar segment was absent. The deep reflexes were extremely sluggish. Sphincter control was absent. A roentgenogram revealed crushed fracture of the posterior process of the first lumbar vertebra, with backward displacement of the body. Spinal puncture between the third and fourth lumbar vertebrae gave fluid which was at first clear and then tinged with blood; there was no rise in pressure on jugular compression. Laminectomy was performed, and the cord found to be edematous; no tear was visible. Suprapubic cystostomy was done later to prevent urinary infection. Three months after injury the patient was able to walk, neurologic conditions were normal, and the suprapubic wound had healed, with consequent return of sphincter control.

KISER, JR., Atlanta, Ga.

AN ANALYSIS OF 2,126 CASES OF ACUTE APPENDICITIS. B. R. SWORN and G. M. FITZGIBBON, Brit. J. Surg. **19**:410 (Jan.) 1932.

A number of tables were presented showing the results of acute appendicitis during the years 1920 to 1929, inclusive. From these results the following conclusions were formed: 1. All cases of acute appendicitis in which no mass is palpable require immediate surgical treatment. Appendectomy carried out during the first twenty-four hours of the disease has a very low rate of mortality. On subsequent days it rises much higher, but according to their findings does not continue to rise after the first forty-eight hours.

2. In cases with diffuse peritonitis, removal of the appendix is essential. If appendectomy is carried out, drainage of the peritoneum seemed of little importance. There is practically no relation between the duration of the disease and the death rate, which is as high on the first day as on any following day.

3. If a palpable mass is present, the best results are obtained by conservative treatment when this is possible. If operative treatment is indicated, drainage alone is the method of choice. After a suitable interval, appendectomy is necessary after the conservative treatment, but in 299 such cases in which operation was performed no deaths occurred.

SUMMERFELDT, Toronto, Canada.

PATHOLOGY AND TREATMENT OF TUBERCULOSIS OF THE KNEE JOINT. G. R. GIRDLESTONE, Brit. J. Surg. **19**:488 (Jan.) 1932.

Tuberculosis of the knee is always secondary to active tuberculosis elsewhere in the body, and the commencement of a focus in or near a joint may be due to tubercle bacilli settling in an area devitalized by a blow or settling in such large numbers that they can survive without preparatory devitalization.

The site of infection of the knee joint may be: (1) the synovial membrane or (2) one or more foci in the bone on either side of the epiphyseal cartilage.

The cases can be classified: (*a*) into three groups by the study of stereoscopic roentgenograms, and again (*b*) into three groups by the age of the patient. In the first classification (*a*) are found the following cases: 1. Extra-articular, with osseous foci irritating but not yet infecting the joint. The treatment is radical elimination of these foci, but one should be sure that there is no communication from the focus to the joint not shown in the roentgenograms. 2. Focal-articular,

with osseous foci opening into the joint and discharging tubercle bacilli into it. Here fusion alone can give security, and the arthrodesis performed at a time which is determined by the age and local and general conditions. 3. Nonfocal, without osseous foci visible by roentgenogram. In such cases in young children there is good hope of recovery with full movement after a long-continued immobilization.

In the second classification (according to the age of the patient) are listed: 1. Children up to 10 years of age for whom prolonged immobilization is indicated, but neither diagnostic arthrotomy nor fusion. 2. Adolescents and adults from 15 to 50 years, healed by immobilization by fusion after the diagnosis has been confirmed by arthrotomy. 3. The elderly, from 50 onward, for whom amputation is usually wiser than fusion.

The clinical diagnosis was discussed and also diagnostic arthrotomy, which is contraindicated until the patient reaches an age when a positive diagnosis of tuberculosis is quickly followed by fusion, which is never done in young children. A positive diagnosis made on clinical grounds is sufficient in the majority of cases.

The treatment consists of general and local measures. As the local signs are only part of the picture, general treatment by means of physical rest, heliotherapy and a well balanced diet is indicated. Local treatment consists of immobilization and operative fusion. These may give the only two safe end-results in tuberculosis of the knee — free movement and bony ankylosis. Arthroplasty has no place in the treatment of tuberculosis of the knee.

SUMMERFELDT, Toronto, Canada.

THE SURGICAL TREATMENT OF CONSTIPATION. H. C. TRUMBLE, M. J. Australia **2**:405 (Oct. 3) 1931.

Trumble presents a preliminary report of his observations on the surgical treatment for constipation based on evidence acquired in animal experimentation and in the course of operations on human beings. His findings in regard to the anatomy of the involuntary nervous system supplying the lower portion of the intestine and the pelvic organs of animals are in agreement with those of Langley, Gaskell, Anderson and others. Fibers arising in the cells of the lumbar segments of the spinal cord pass by way of the white rami from the upper lumbar nerves to the lateral sympathetic chain and then by way of the lumbar splanchnic nerves to the inferior mesenteric ganglion situated in the mesentery of the colon near the origin of the inferior mesenteric artery from the aorta. Here the fibers from each side decussate freely. This ganglion (inferior mesenteric ganglion) gives off (1) branches to the colon, (2) a nerve passing upward in front of the aorta to the celiac plexus and (3) the hypogastric nerves, which pass downward in front of the aorta to the pelvis where they join branches issuing from the second and third sacral nerves to form the pelvic plexus. From the pelvic plexus branches pass to the colon, bladder, rectum and various pelvic viscera. The lumbar sympathetic trunk below the point of outflow of the lumbar splanchnics contains no fibers, or only a few, destined to supply any of the pelvic or abdominal viscera. The author's studies lead him to believe that the general plan of the anatomy of the involuntary nervous system in animals is similar to that in human beings, and he consequently makes a plea for the revision of standard textbooks in which the nomenclature and descriptions of the anatomy of the abdominal involuntary nerves are both confusing and inaccurate.

In regard to the physiology of the neuromuscular mechanism of the lower part of the intestine the author makes the following statements. The pelvic visceral nerves control mass evacuation of the distal colon, stimulation of them under certain conditions causing powerful contractions of the circular and longitudinal muscle coats and relaxation of the retaining sphincters. Section of the pelvic nerves is followed by some dilatation of the lower portion of the colon, and emptying of it is brought about by a series of ordinary peristaltic waves causing the expulsion of small amounts of stool at frequent intervals. On the other hand, stimulation of the lumbar splanchnic nerve or of the branches of the inferior mesenteric

ganglion causes inhibition of the circular and longitudinal coats of the colonic musculature and contraction of the internal anal sphincter. When the abdomen of an animal or man is opened, it is uncommon to observe any movement of the colon, and even stimulation of the pelvic nerves in the experimental animal may fail to bring about active peristaltic movements until after the lumbar splanchnic nerves have been divided. If the lumbar splanchnics or branches of the inferior mesenteric ganglion in animals are divided, active peristaltic movements appear either spontaneously or as the result of various forms of stimulation. It would appear that with the splanchnic nerves intact there is active reflex inhibition of colonic musculature and that section of the nerves destroys the arcs on which the reflex depends.

With these facts in mind the author explains Hirschsprung's disease and other conditions characterized by obstinate constipation and inert colonic musculature by assuming that there is at work an active reflex which effects inhibition of the musculature of the colonic wall, together with increased tone of the retaining sphincters. This abnormal reflex activity may be excited by some pathologic state in the intestine or elsewhere in the body acting as a focus for the generation of sensory impulses, or the arc itself may be abnormally sensitive so that it reacts in an exaggerated fashion to stimuli that would, as a rule, produce little effect. The local nervous derangement may be part of a widespread condition akin to neurasthenia. Finally this abnormal sensibility may be secondary to some abnormality of control of the reflex by fibers from the hypothalamus. Whatever may be the explanation of this excessive reflex activity of the lumbar sympathetic outflow, section of fibers entering into the formation of the arcs concerned should destroy the reflex arc, abolish the nervous effect and leave the muscles of the colonic wall free from active interference. The author then describes a new operation designed to effect this "release" of the intestine. It consists of a division of the lumbar splanchnic nerves just proximal to the inferior mesenteric ganglion. It differs from the operations of Wade and Judd and Adson in that it is bilateral in its effect and in that, by making the division of the involuntary nerve supply to the lower part of the abdomen and pelvis close to the viscera involved, it avoids unnecessary division of a large number of unconcerned trunks, especially the sympathetic supply to the legs. Reports of five cases in which the operation was performed with satisfactory results are included and discussed.

GONCE, Madison.

CLUTTON'S JOINTS. G. T. MULLALLY, Proc. Roy. Soc. Med. **24**:1182 (July) 1931.

A painless effusion in the left knee followed a fall four days previously. Roentgen examination gave negative results. The Wassermann reaction was two plus. On further examination there were found to be characteristic changes in the teeth and scarring at the corners of the mouth.

WILLIAMSON, New Orleans.

TERATOMA OF OVARY. DUNCAN FITZWILLIAMS, Proc. Roy. Soc. Med. **24**:1342 (Aug.) 1931.

A girl, aged 9 years, was admitted to the hospital on account of an increasing abdominal swelling which had been noticed about three weeks. A tumor extending from the pelvis to the umbilicus and into both iliac fossae was palpable. It was irregular in outline, nodular and firm in consistence. A pedunculated tumor rising out of the pelvis, originating in the right ovary and filling the superior outlet of the pelvis was removed by operation. In some parts it was cystic in consistency; in others, as hard as bone. The patient made an uneventful recovery.

WILLIAMSON, New Orleans.

THE COURSE AND TREATMENT OF EMPYEMA IN CHILDHOOD. H. FRENKIEL and A. MARGOLIS, Monatschr. f. Kinderh. **51**:188 (Oct. 31) 1931.

The authors report a very high mortality in their cases of empyema. Of the patients under 1 year of age, 73 per cent died; of those from 1 to 2 years old, 69 per cent; of those from 2 to 4 years old, 39 per cent; of those from 4 to 8 years old, 27 per cent, and of those over 8 years, 12 per cent. The mortality according to organisms was: Streptococcus pyogenes, 37 per cent, the pneumococcus 49 per cent; mixed infections, 49 per cent; Streptococcus mucosus, 54 per cent, and Staphylococcus pyogenes, 61 per cent. The treatment was classed as conservative and surgical. The conservative consisted of punctures and lavage; surgical measures included the open and closed methods. In 26 per cent conservative measures were successful; 61 per cent of those who recovered needed a secondary operation to establish permanent cure. In the conservatively handled cases, lavage with ethylhydrocupreine solution seemed of some value, but the authors do not believe that the drug itself really had any effect, and are somewhat afraid of it. Of surgical procedures they much prefer the closed method.

GERSTLEY, Chicago.

Miscellaneous

THE SEASONAL INCIDENCE OF SOME OF THE DISEASES OF CHILDHOOD. CHARLES HERRMAN, Arch. Pediat. **49**:73 (Feb.) 1932.

Attention is called to the rather large number of conditions, infectious and otherwise, occurring during the later winter and early spring months. Some of the literature pertaining to this subject is reviewed. The writer calls attention to the fact that human beings are subject to many of the same biologic laws as plants and animals, and points out that the physical, physiologic and chemical conditions of the body differ at different seasons of the year. As several functional neuroses and constitutional conditions as well as infectious diseases present this seasonal incidence, it seems unlikely that an increased virulence of infectious material is the primary etiologic factor. The writer suspects that the injurious effect may depend on a sudden transition or an abrupt change in some meteorologic element, and that there are certain persons who are unable to adjust themselves quickly to these sudden changes. The solution of these problems will require the combined efforts of biologists, physicists and physicians. The writer feels that it is advisable to provide infants, children and pregnant and lactating mothers with a diet containing an adequate amount of vitamins, and to expose them outdoors in the winter and spring so that they may increase their ability to adjust themselves rapidly to sudden changes of climate. This method of prophylaxis is compared to desensitization to certain foodstuffs in persons who have an idiosyncrasy or to the gradual development of acquired immunity by exposure to small doses of the infectious material.

WADDELL, JR., University, Va.

CONVALESCENT CARE FOR HOSPITAL BABIES. HENRY DWIGHT CHAPIN, J. A. M. A. **98**:40 (Jan. 2) 1932.

Babies are kept too long in hospitals and are not sufficiently overseen after discharge to insure permanent benefit. The place that is good for treating disease is not a good place for convalescents. Delay in discharge often defeats the benefit of hospital treatment. The interim between hospital care and the return home is the neglected time. The dangers of cross-infections, insufficient fresh air and rotation of interns and nurses are accompaniments of institutional care. When the hospital ceases its ministrations, it is best for the infant to be placed in a family. This is the plan that the author devised. The foster-mothers are instructed and the infants followed up by physician and nurses. Each unit is operated uniformly,

and admissions are arranged by the convalescent service of the United Hospital Fund of New York. In 1930, there were 1,088 patients of whom 795 were discharged cured. The daily cost per capita was $1.64.

BONAR, Salt Lake City.

ROENGENOLOGIC DIAGNOSIS OF LEAD POISONING IN INFANTS AND CHILDREN. EDWARD C. VOGT, J. A. M. A. **98**:125 (Jan. 9) 1932.

Lead poisoning in infants and children is usually the result of chewing paint from furniture, woodwork, toys and nipple shields. Gastro-intestinal and obscure neurologic complaints are the symptoms. When absorbed into the body, lead may be found stored in the bones. Roentgenograms reveal a dense band at the growing margins, which, however, is not pathognomonic. Its elimination can be followed roentgenologically.

BONAR, Salt Lake City.

THE INFANT MORTALITY OF BIRTH. THOMAS WATTS EDEN, Lancet **2**:1223 (Dec. 5) 1931.

The stillbirth rate in England averages between 33 and 35 per thousand births. The neonatal mortality (during the first four weeks of life) has shown a slowly progressive diminution (31 per thousand births in 1930), but it has lagged behind the fall in rate for the whole year. This neonatal mortality is a matter of grave concern, as a considerable proportion is undoubtedly due to the results of obstetric trauma.

Roughly, 20 per cent of the total stillbirth mortality in the lying-in hospitals is attributable directly to birth trauma. Breech presentation and occiput posterior presentation of the vertex are the two conditions that most often lead to fetal disaster. Gibberd estimated the total intranatal (30 per cent) and neonatal (9 per cent) deaths in all cases of breech presentation as 39 per cent. (This high figure is inapplicable generally, owing to the high proportion of complex cases treated in these lying-in hospitals.) It is difficult to estimate the extent to which the life of the child was already prejudiced by conditions that necessitated the use of forceps; however, the operation in its simplest form is attended by definite risk to the life of the infant.

Of Cruickshank's 800 cases of neonatal death, 70.6 per cent occurred during the first week. In all, 540 of the 800 cases were attributable in whole or in part to asphyxia. In 161, gross intracranial bleeding was found. Delayed effects of trauma, such as palsies, were not considered in this article.

To what extent is the mortality avoidable? Deaths due to toxemia are almost entirely preventable by systematic antenatal supervision and treatment, but ignorance of the cause of premature birth and of placenta praevia is profound.

Is it not possible that obstetric methods do not take sufficient account of the vulnerability of the infant? Experiments on rats have shown that deficiency in vitamin E in the maternal diet has a marked influence on fetal development. Vitamins D and A also play an important rôle, as proved experimentally.

LANGMANN, New York.

SOME OBSERVATIONS ON BROMIDE THERAPY AND INTOXICATION. CLIVE SIPPE and JOHN BOSTOCH, M. J. Australia **1**:85 (Jan. 16) 1932.

As bromides replace the sodium chloride in the blood, the bromide concentration increasing as the percentage of sodium chloride diminishes and the reverse happening as the bromide is excreted, and as the elimination of bromides is helped by the intake of sodium chloride, the replacement of the sodium chloride by bromides during the administration of bromides depends to a certain extent on the amount of salt in the patient's diet. A dose toxic to a patient on a low intake of salt could be harmless and useless to one on a high intake of chloride. Consequently,

estimation of the bromide in the blood is of value in controlling bromide therapy. However, the tolerance to bromides varies in different persons, the optimum concentration in the blood ranging between 100 and 225 mg. per hundred cubic centimeters. In many cases levels above 200 mg. give rise to toxic symptoms. Symptoms of bromide intoxication are protean, and include somnolence, fatigue, loss of energy, inability to concentrate, staggering gait, a feeling of being drunk, hallucinations, delusions, disorientation as to time and place, emotional depression and sometimes acute mania. Little attention should be paid to the rash as an indication of toxicity, as the other signs are more important and common. Too rapid withdrawal of bromides and too rapid use of chlorides after withdrawal of bromides in cases of intoxication are contraindicated.

GONCE, Madison, Wis.

HYPERPYREXIAL HEATSTROKE: A MESOPOTAMIAN EXPERIENCE, WITH SOME ETIOLOGIC VIEWS AND A METHOD OF PREVENTION RESULTING THEREFROM. K. S. HEARNE, M. J. Australia **1**:226 (Feb. 13) 1932.

While stationed at Basra with the British Expeditionary Forces in Mesopotamia in the summer of 1917, the author had the opportunity of studying about 240 cases of true hyperpyrexial heatstroke. The principal features of this condition are hyperpyrexia, a dry skin, the sudden appearance of mental excitement and delirium passing rapidly into unconsciousness and coma, labored and stertorous breathing and convulsions of the epileptiform type.

The author feels that the cause of heatstroke is suppression of perspiration, which invariably precedes the attack for a more or less considerable time. There being no surface moisture available, the body is not only deprived of its power to lose internally produced heat but actually gains heat from the surrounding atmosphere which may be from 30 to 40 F. higher than the normal temperature of the body. The brain and tissues rapidly become superheated, which results in typical convulsions, coma and death if the patient is not subjected to early treatment.

The universal observation that frequency of urination occurs before the attack was also noted by the author. He believes this feature of the condition to be the result of the suppression of sweating, and proof that suppression of sweating precedes the attack by some time. Pilocarpine given subcutaneously to 10 patients with heatstroke did not produce the least trace of perspiration, though the salivary glands responded with profuse salivation. This seems to indicate a definite failure of the sweating mechanism, and the author suggests that the failure is due to exhaustion of this mechanism brought about by several previous days of extreme hyperactivity.

By having hospital patients and soldiers on duty report immediately any frequency of micturition or stoppage of sweating, the author was able to prevent heatstroke by the simple process of artificially supplying moisture to the surface of the skin. "If the patient's temperature were 39.4 C. (103 F.) or more, he would be stripped and covered with a sheet which would be sprayed at intervals with just sufficient ice water to keep the sheet moist without damaging the mattress. Evaporation was assisted by the current of air from the overhead electric punkas which sufficed to keep the patient's temperature under control until after sundown, when the intensity of the day's heat generally abated, rendering further protection for that day unnecessary. There were, however, a few cases in which a portable electric fan at the bedside was also required, and occasionally it was found necessary to continue the wet sheet treatment until late in the night."

GONCE, Madison, Wis.

LACTOGOGIC ACTION OF ULTRAVIOLET RAYS. AXENTE IANCOU and I. IANA, Bull. Soc. de pédiat. de Paris **29**:423 (July) 1931.

Numerous conflicting reports as to the value of ultraviolet irradiation as a galactogogue are cited. The authors attempted to determine the truth in the

matter by giving ultraviolet exposures to a series of twenty-five nursing mothers. Fourteen of this number showed increased secretion of breast milk; five doubled the quantities of milk which they had secreted before the actinic therapy was begun. It is difficult to evaluate the results of treatment because of many uncontrollable factors, such as the age of the mother, the number of previous pregnancies and the anatomic differences of breasts. It is these various factors which account for the discrepancies in the reports.

BENJAMIN, Montreal, Canada.

OBJECTIVE EVALUATION OF THE RESULTS OF VACATIONS AND REST CURES. E. SCHLESINGER, Gesundhfürs. f. d. Kindesalt. **6**:245 (Sept.) 1931.

The author has attempted to study methods by which the evaluation of the results of vacations and rest cures can be arrived at by objective measures. The weight must be studied critically, and an attempt should be made to differentiate between mere development of fat and increase in muscle and bone. In the case of rest cures one often finds an accentuation of the normal variations in weight due to seasonal changes. It was interesting to observe that overweight children tended to decrease in weight, although subsequently the excess weight was regained. The author advises the use of Collin's dynamometer and the spirometer. The results of these examinations show, according to the author, that the increase in height is due to the elimination of school work. There is a definite increase in the circumference of the chest in inspiration; this is probably due to the life in the open air. The development of weight depends on stimulations due to change in climate, weather and environment. The increase in vital capacity depends on training in sports. In general, much better results were obtained when children went to organized convalescent homes than when they were permitted to go to private establishments or families.

REICHLE, Cleveland.

DIFFICULTIES IN THE USE OF MORTALITY STATISTICS IN INFANCY. E. BURGHARD, Gesundhfürs. f. d. Kindesalt. **6**:327 (Nov.) 1931.

The author shows the errors that arise from the superficial examination of mortality statistics.

REICHLE, Cleveland.

STANDING IN INFANCY. A. PEIPER, Jahrb. f. Kinderh. **134**:149 (Jan.) 1932.

While the infant is acquiring the upright gait, reflexes appear which are fundamentally like those in quadrupeds. These reactions include the ability to stand, reactions of support, changes in the tonus of support due to movements of the head, reflexes of the vertebral column, the effect on tonus of an extremity, due to the position of the opposite extremity, and retraction of the arms. The infant passes through the stage of the quadruped; when placed on the abdomen, both use the upper extremities to support the body and to move it forward. At this time, the same reflexes may be demonstrated in the arm of the child and the foreleg of the animal. Gradually changes appear as the human subject acquires the erect posture. Then the supporting reflex of the arm is lost, while the grasping reflex develops.

CLAUSEN, Rochester, N. Y.

STATISTICS ON INFANT MORTALITY PER THOUSAND BIRTHS IN THE MOST IMPORTANT COUNTRIES OF THE WORLD. K. RYDER, Opieka nad dzieckiem **7**:77 (March-June) 1929.

In thirty-one of the most important countries of the world the death rate decreased from 1879 to 1923, with the exception of Ceylon, Rumania, Jamaica, Prussia, Japan and Russia.

KRUPINSKI, Chicago.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

JOHN CAFFEY, M.D., *Secretary*

March 10, 1932

HERBERT B. WILCOX, M.D., *Presiding*

RADIATION IN THE TREATMENT OF DISEASE. ETHEL M. LUCE-CLAUSEN.

A historical sketch was given of the pioneer investigations on light, dating from the work of Home, 1820, to show that studies of the period from 1820 to 1890 gave us some fundamental facts concerning light on which we have been building ever since. The clinical aspects of radiation therapy were then discussed, with special reference to the use of sunlight and artificial sources of light in the treatment of wounds, of cutaneous diseases, of tuberculosis and of rickets and tetany. It was emphasized that in the treatment of the two latter diseases only could light be described as a specific. An account was then given of experiments being conducted in Rochester, in collaboration with L. A. Jones of Kodak Park, involving the use of isolated radiations and their effect on the growth of both rachitic and normal rats. Certain interesting effects of infra-red radiation (700 to 1,120 millimicrons) were discussed. These rays have been found to interfere with the full calcifying effect, on rachitic rats, of an isolated group of rays in the ultraviolet rays. It was suggested that we might be dealing here with a biologic parallel of the Herschell effect known in photography. Growth-promoting effects of these infra-red rays on normal rats were also demonstrated. The importance of differentiating between effects of energy supplied by infra-red radiation and those supplied by raising the temperature of the air was emphasized, and certain experiments along these lines being carried on at the present time were described.

DISCUSSION

DR. ALFRED F. HESS: Although Dr. Luce-Clausen has made apologies for not being able to solve some of the fundamentals of the question, I hope you will realize that she has tackled the problem of the value and action of infra-red rays better and more fully than any one else. I shall take up some of the questions she has raised.

The action of ultraviolet light on tuberculosis has always been interesting to clinicians. It is increasingly evident that light is to a definite degree curative in tuberculous peritonitis. This fact leads one on to experiment in the field. Light is also extensively used in lupus in Rollier's clinic.

I carried out some experiments on guinea-pigs with much the same results as Dr. Luce-Clausen obtained. The animals not only were not protected by various degrees of ultraviolet light, but were made worse. We tried to desensitize them with some tubercle bacilli, but were unable to accomplish it. If anybody can produce a localized or a chronic tuberculosis in an animal, this field will be open for experimentation. Some have tried to produce tuberculosis of the eye, but I believe that this problem can be solved if some immunologic trick, perhaps, is made use of.

Two years ago, I saw men at Rollier's clinic in Copenhagen working with lupus and trying to find out just what wavelengths or bands were active in the cure, but they had not advanced far. I came back with some such idea, but I understand that lupus is a much rarer disease in this country than in Copenhagen.

In regard to rickets, it is now an old subject. Subjects get old so quickly nowadays. There is so much literature, and so many people are working on rickets. One thing must be attributed to this condition, that is, all this interest in light. Until we could really prove clinically, experimentally and objectively, by roentgen rays and by chemistry, that light cured something, the whole study savored of charlatanism. In fact, when I began this study, it was almost as much as my reputation was worth to say that light was curative. A colleague patted me on the shoulder and said, "Hess, that is just a psychological effect." No doubt, though, the theory that light was curative led to all these studies, but how it works we do not know now any more than we knew at the beginning. As a matter of fact, we do not know much about how anything works. Although we know more about tricks today than they did in Lister's time, we do not know any more about the pathogenics of rickets.

Regarding monochromatic light, it can be studied this way, but the energy value is so slight that one cannot do any work with it. Recently some work has been done in Uppsala, Sweden, in regard to the active principle that protects against scurvy. But this work has not been confirmed. Probably there are some other specific actions of these rays.

As regards the clinical applications of light, there are some things that I think we know clinically which cannot be proved. There are some children who seem to have a sense of well-being after having been treated with a mercury vapor lamp or a carbon arc lamp; this seems to be definite. Then light is used for the same kind of condition in another child and there is no result. I think, however, that the cases are probably not the same kind, that the diagnosis has been improper. Everybody has had this kind of experience. There must be some clinical conditions in addition to rickets that are benefited in this way.

As you know, these lamps are lauded for conditions for which they have no value. I want to mention colds. I can speak with some positiveness about this matter, because for two years we used lamps in trying to prevent colds and respiratory infections, which are the great menace of child-caring institutions. For one year we used radiation by mercury vapor lamp in half of one ward, and for one year radiation by carbon arc lamp in half of another ward. In both years the number of respiratory infections was about the same among the irradiated as among the unirradiated group.

Radiation is of value, however, not only for rickets, but also when there is a lack of calcification. It is of value in pregnancy, especially for the fetus. It is of value in lactation both for the mother and the child. It can be proved that if the mother is irradiated great potency is conferred on the milk. Milk that will not protect a guinea-pig, after irradiation of the mother will give protection if only 5 cc. of it is ingested.

We performed some other experiments with infra-red rays. About ten years ago, we first found that if the ultraviolet light is used and a burn results, one can to a certain extent nullify this action by using at the same time infra-red light. It is necessary to work until the right degree for neutralization is attained. We had some experience with rats; they could not stand the heat, and they sweat profusely. It is remarkable how wet they became. We found in this way that the infra-red interfered with the ultraviolet rays, and afterward we did the same thing with gastrula.

Dr. Luce-Clausen said nothing about her expirements with thyroid. I remember she published some interesting work in regard to the effect of the infra-red ray on the size of the thyroid and parathyroid glands.

Finally, in regard to the sensitization, it is interesting, but I do not know that there is proof that the ultraviolet rays has much to do with it. There is the effect on buckwheat. In certain districts in the summer in which buckwheat is grown there were only black cattle, because the white cattle died from the sensitizing effect of the light. Then there is the effect that quinine creates; it will sensitize to light and lead to blindness.

There are probably some other factors in the diet that make us more or less sensitive to sunlight.

This whole question of the use of filters has never been as carefully presented as it was this evening.

DR. E. E. FREE: It is unusual and exceedingly refreshing to a physicist to listen to a paper like the one we have listened to this evening, in which the physical aspects of the problem have been adequately considered, because under the compulsion of reading a good many miles of literature on ultraviolet rays in which no attention had been paid to the physical fundamentals, I have become convinced that some adequate attention should be given to them. You have heard a paper in which that phase of the problem has been practically carried out, and remarks by Dr. Hess, who is a pioneer of physical control as well as of the biologic aspects of the work. Part of the confusion that upsets the whole field of biologic effort is due to the fact that the physical factors have not been adequately considered. In this instance, there is no such criticism to be made.

It is interesting to point out that the science of physics is not yet able to give the biologist a proper method. There are only two methods available for acquiring monochromatic light. One is the filter method that Dr. Luce-Clausen has used, which has serious disadvantages. The other method has been used in my laboratory. We built as large a spectroscope as possible to get as pure irradiation as possible. But there is difficulty always with either of these methods. If the filter method is used, which I think is the better of the two, there is the disadvantage that if the filter is small enough, the energy is insufficient. If one selects, as I did, the method of building the largest monochromatic illuminator that can be built, there are equal disadvantages, such as stray light and the like. So our results are open all the time to the criticisms that we are not using enough energy to get effects and that we are not using pure energy. The amount of energy we get is about one mosquito power. With this we cannot do anything chemically, let alone biologically.

There is one method of investigation that promises to yield an improved technic. It is a method that I should like to see some well equipped laboratory take up. This is the possibility of using a gaseous spectrum to produce monochromatic radiation. Sodium lime is no good for these things. It ought to be possible to devise lamps which will produce many times the amount of energy that we can now get. Concerning the matter of specific effects, we are coming to believe less and less in these specific effects proved not on the basis of biologic evidence, but on the basis of photochemical evidence.

There are two factors that produce the reaction: (1) absorption and (2) energy in the absorbed wavelength, although the wavelength itself as a factor is minor. We have pretty definitely proved that.

I am tempted to say more than I should about the theory of the effects that we as physicists and chemists have formulated, although it is a theory that belongs in the medical field. It seems to me more and more likely that there may be something in it. Let us ignore for the purposes of this discussion the simple matter of rickets. Let us consider the biologic effect on any organism of any form of radiation, assuming of course that the organism absorbs the radiation. We have done nothing except with low organisms. There is one effect that we know occurs to every organism, whatever the kind of radiation, and that is destruction of tissues. There is a threshold of energy tension below which no destruction of tissue takes place. Any organism can be killed by sufficient intensity of radiation. We infer that destruction of living matter has on any organism a more or less standard effect. If it is not too great, the effect is stimulating. If it is too great, the effect is depressant. That applies to virtually all agents. Now there is a simple way to explain all of these effects. This explanation may not be correct, because it is too simple. Take, for instance, tuberculosis; Dr. Luce-Clausen has said that the effect of any form of radiation on tuberculosis is not always beneficial. It is frequently harmful. If we assume that the fundamental principle is the destruction of tissue, then the effect will be determined

by two things; first, the intensity of tissue destruction and, second, the speed with which the destruction is eliminated from the organism. As in rheumatism, if the burn is slight, we get improvement; if the burn is great, we get a harmful effect. The eliminating process is too slow. I am frank enough to say that as a physicist and chemist I have never seen any report of adequately controlled experimental data in this field that could not be explained on this basis. I think all of Dr. Luce-Clausen's results can be so explained. For example, the harmful effect of infra-red radiation is due perhaps to the fact that it produces too much destruction. Of course temperature effects and absorption effects come in. Furthermore, there is an important effect to be watched for in these things, judging by our chemical and micro-organism work, which may or may not be important. It is seldom that any one observes the transparency of the filters in experimental radiation. It is difficult, almost impossible, to make those observations with our present physical equipment. Dr. Jones has the best equipment I know of. Any filter that one uses heats up and then becomes a secondary source of infra-red radiation. This may affect some of the phenomena concerned, although of course that is merely a general suggestion. I do not know what to do about it. It is possible to produce any wavelength, but not possible to produce radiation reasonably free from this effect. So the problem becomes one of the most extreme experimental difficulties, a statement which, of course, can be applied to everything in this field.

Now as to antagonism, there is a possibility of its being something worth considering. Take the specific matter of the apparent antagonism between actinic and infra-red rays. That effect is that of making a photograph on a plate; one produces a latent image. It can be wiped out by exposing the plate to infra-red radiation. Take a simple case, a crystal of silver bromide. The action is to detach one electron and hold it off. The production of the latent image is something of that general sort. I imagine that is what happens when infra-red radiation gets on this structure. It heats all kinds of structures definitely and locally. Uniformly the effect is to let the electron go back where it was. It seems to me that that is a plausible explanation. It is not my own belief but that of a German physicist. My belief is that possibly the effect applies to the antagonism that perhaps exists between the activation of such products as ergosterol. It is some sort of partial lessening or change or atomic alteration in the lipoid. The molecule is changed by the radiation, not in chemical constituency, but in structure. If one assumes that it is then acted on by heat, naturally the molecule should return to its primary condition. I am not sure that this happens in ergosterol, but it may.

In conclusion, let me say again I think that we have listened to a most admirable presentation of an important and admirable piece of work from the physicist's standpoint.

CHICAGO PEDIATRIC SOCIETY

Regular Meeting, April 19, 1932

HENRY E. IRISH, M. D., *President, in the Chair*

THE SIGNIFICANCE OF OBSCURE ABDOMINAL PAIN IN THE OLDER CHILD. DR. FREDERIC W. SCHLUTZ.

Persistent, vague abdominal pains are a comparatively frequent complaint in the older child. The pain occurs periodically, is of variable duration and at times is intense during the attack. It is entirely too intense to be ascribed to psychic, emotional or environmental factors. The location is usually umbilical or in the right lower abdominal quadrant. These children are generally free from acute or chronic alimentary disease and are often in a good state of nutrition. A striking feature is the great infrequency of acute or chronic organic disease.

In forty-five cases of chronic abdominal pain taken at random from the hospital files of the pediatric department, the age of the patients, except in three cases, ranged from 5 to 14 years. There were sixteen male and twenty-seven female patients. The length of time of complaint dated from one month to seven years. The pains were momentary or prolonged, and occurred daily or at less frequent intervals.

The nutritional state of most of the children was generally fair or even good. About 15 per cent of the cases were of the asthenic type. Syphilis or acute or chronic forms of tuberculosis, as evidenced by the Mantoux test and by roentgenograms, were found in only four cases. In none of the cases was there abdominal or peritoneal tuberculosis. Tabes mesenterica was found in three patients, all of whom were females. Chronic pulmonary nontuberculous conditions were found in only two cases. Chronic cardiac disease was found in two cases, and enlargement of the liver and spleen in two others. Acute or chronic appendicitis had been diagnosed in six of the cases, and in two of them appendectomy had been performed. Pyelocystitis was found in six cases; none of these cases showed urinary anomaly. In two cases there was renal stone. Pelvic disease was found once in an older girl, and was probably due to a cyst. Gastric or duodenal ulcer was found in two cases, both in boys, one aged 14½ years and the other 8 years.

In practically none of the patients were there febrile reactions. About 30 per cent of the children gave a history of dietary indiscretion, improper food intake or bad dietary habits. Psychic and emotional factors were not dominant in over two thirds of the group. Twenty-five per cent of the cases showed chronic constipation, and only three cases an occasional diarrhea. Over 40 per cent of them showed occasional nausea and vomiting. In only two cases were there a history and finding of intestinal parasites.

The outstanding feature in this condition is the relative absence of real organic disease, either enteral or para-enteral. That it is occasionally found and must be sought for is illustrated by four cases.

Case 1.—This was a case of proved duodenal ulcer in a boy, aged 14½ years, in whom the condition had lasted for seven years. An appendectomy had been performed on this boy, followed by nonrelief of symptoms. Ulcer management and a Sippy diet apparently completely relieved the disorder.

Case 2.—The case concerns a girl, aged 10 years, who had complained of abdominal pain for the past five years. A persistent tender area about the umbilical region proved the pain to be due to a strangulated umbilical hernia. This was removed, and the child has been entirely free from any complaint since the operation.

Case 3.—The case concerns a boy, aged 14 years, who complained of abdominal and lumbodorsal pain for the past two years. The pains were commonly accompanied by hematuria. Roentgen examination revealed a large stone in the left kidney, which was removed by nephrotomy. There was complete recovery, and no complaint of pain has been made since the operation.

Case 4.—The case concerns a child of 16 months who complained of vague abdominal pains and a persistent pyelitis since early infancy. A test with iopax and roentgen examination of the genito-urinary tract revealed a small renal calculus in the left kidney. This was removed by nephrotomy, and the child made a complete recovery.

The pathologic condition in these cases, if no organic cause can be found, is generally meteorism. Practically all the patients were relieved by dietary management consisting of a high protein, low residue diet and the use of preparations containing belladonna.

Acute Leukemia Following Lymphosarcoma. Dr. Katsuji Kato.

The cases presented here illustrate a peculiar combination of symptoms and course, beginning with localized lymphosarcomas, treated with deep roentgen

irradiation, and terminating with acute lymphatic leukemia. The first case is from the University of Chicago Clinics. A girl, aged 4½ years, came with a complaint of a firm, nonfluctuating tumor mass of the left side of the face, which was diagnosed as lymphosarcoma (Paltauf type) by biopsy from a lymph gland in the swollen area. Five deep roentgenotherapies at two day intervals completely reduced the swelling. The patient was apparently well for four weeks but again returned to the hospital with the typical picture of acute lymphatic leukemia. Autopsy confirmed the diagnosis, although the lymphocytic hyperplasia was limited to the organs of the lymphatic system. The second case was that of a boy, aged 9 years, who was brought to the Children's Memorial Hospital with marked respiratory embarrassment. The child had a tumor of the sternum on the anterior wall of the chest, and the roentgenogram revealed a massive mediastinal lymphosarcoma with pleural exudate on the left side. Deep roentgenotherapy brought about a rapid improvement in the general condition, and the mediastinal mass disappeared in ten days. Thirteen days after discharge from the hospital, typical signs of acute lymphatic leukemia developed, which terminated fatally within a week. From the study of these cases, two tentative conclusions seem warranted: 1. The employment of roentgen irradiation in the treatment of this type of lymphosarcoma and leukemia may be questioned. 2. Lymphosarcoma is a precursor of lymphatic leukemia, and the two conditions are merely different phases of neoplastic lymphoblastosis of extremely malignant type.

THE TREATMENT OF NUTRITIONAL ANEMIA IN INFANTS WITH COPPER AND IRON. DR. BENGT HAMILTON.

According to Josephs, the anemias are divided into those due to increased destruction of blood and those due to decreased formation of blood. In the former, when destruction of blood is increased, as, for instance, in syphilis, tuberculosis and the like, the important thing is to remove the cause of the destruction, if possible. Treatment with copper and iron are rarely successful until the primary factor has been removed.

In anemia due to decreased formation of blood, the cases due to aplastic bone marrow or destruction of the bone marrow, as in leukemia, do not, of course, respond to treatment with copper and iron. In cases in which prolonged milk feeding has led to severe anemia, often further aggravated by repeated infections, the copper and iron treatment gives exceedingly good results. The form of treatment used is that recommended by Josephs; copper sulphate, 0.5 per cent solution, 1 cc. per kilogram per day up to 10 cc. and ferric ammonium citrate, 10 per cent solution, 2 cc. per kilogram per day. Both solutions are to be given in milk.

The copper is given for about ten days; then the treatment is continued with iron alone.

Cases were presented illustrating the rapid rise of hemoglobin when this treatment was appropriately used.

THE HISTAMINE TEST OF GASTRIC SECRETION IN CHILDHOOD. DR. WALTER J. SIEMSEN.

This article will be published in full in a later issue.

MINERAL COMPOSITION OF THE OFFSPRING AFTER FEEDING COD LIVER OIL AND VIOSTEROL TO THE MOTHER RAT. DRS. W. W. SWANSON and L. VIVIAN IOB.

The object of this study was to find additional evidence of nutritional improvement in the offspring after feeding the mother rat cod liver oil or viosterol during gestation. Apparently the general impression to be obtained from the

reading of various papers is that an increase in vitamin D in the mother's diet does benefit the offspring. Korenchevsky, in 1923, came to the following conclusions, based on feeding experiments with rats:

1. A sufficiency of the fat-soluble factor improves nutrition in the offspring and resists rachitic changes for a longer period of time when the rat, after weaning, is kept on a diet deficient in the fat-soluble factor.

2. There also appears to be a protective influence tending to prevent later nutritional and rachitic changes if the fat-soluble factor is abundant in the mother's diet during lactation.

The Influence of Cod Liver Oil and Viosterol on the Mineral Composition of the New-Born Rat *

Diet of Mother	No. of Litters	Aver. No. in Litter	Aver. Wt. per Rat, Gm.	Phosphorus	Calcium	Magnesium	Sodium	Potassium	Chlorine	Nitrogen, Gm.
Control	10	8.6	5.627	601	482	62.7	585	399	396	109.8
Control + 0.2 cc. cod liver oil	5	9.6	5.519	706	559	67.6	572	397	391	112.7
Control + 0.4 cc. cod liver oil	5	8.4	5.695	652	503	63.9	558	411	389	111.6
Control + 2 drops viosterol	5	9.2	5.538	644	453	64.9	574	404	403	110.0
Control + 4 drops viosterol	5	10.0	5.642	696	549	68.2	622	408	427	116.4

* Values, with the exception of nitrogen, expressed in millimols per kilogram of water-free, fat-free substance.

Hess and Weinstock, in 1924, interpreted their findings as indicating that rickets cannot be prevented by improving the diet of the rat (1) previous to pregnancy, (2) during gestation or (3) by giving cod liver oil during lactation. They concede, however, that the development of rickets may be retarded and mitigated to a certain degree.

In this study on the mineral composition of the offspring after feeding the mother rat cod liver oil and viosterol, the data appear to show an improvement in skeletal growth. There is a definite increase in both phosphorus and calcium. It appears that 0.2 cc. of cod liver oil or four drops of viosterol was the optimal dose. However, this may be a chance finding, since the number analyzed is small. The other minerals are scarcely influenced at all. The accompanying table gives the findings in detail.

Book Reviews

Growth and Development of the Child. Part III. Nutrition. Committee on Growth and Development, White House Conference. Price, $4. Pp. 532. New York: Century Company, 1932.

This volume, which comes as a result of the work of the Committee on Growth and Development of the White House Conference, is an outstanding contribution to the medical literature.

In days when we are receiving so many assurances that this or that type of food is just the thing for all our ailments, it is refreshing and enlightening to have a group of the most outstanding men in the country call attention to the fact that while there are a few things we do know, there are many things we do not know. The care with which all evidence has been valued and the conservatism with which it has been placed in this volume merit praise that could scarcely be too much. The whole subject of nutrition as pertaining to the child is reviewed, and the basic facts are set down. Not only are the facts carefully noted, but just as carefully are shown the loopholes in the knowledge and the way in which these can be filled.

One cannot say that any one chapter in this book is better than another, but of especial interest, considering the present propaganda, are the excellent chapters on vitamins.

To the physician who wishes to ground himself in the matter of the nutrition of the child, this book is invaluable. If a layman could understand it, it would be most useful to curb the enthusiasm for the various products that are being put on the market.

The book is complete and is masterfully written. It is the most important contribution to our knowledge of the subject that has appeared for some time.

Directory of Pediatric Societies

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor Taillens, Lausanne, Switzerland.
Secretary: Dr. P. Oltramare, rue Decandolle, Geneva, Switzerland.

International Pediatric Congress

President: Dr. George Frederic Still, 28 Queen Anne St., London, W. 1.

FOREIGN

Royal Society of Medicine, Section for the Study of Disease in Children

President: Sir Henry Gauvain, 125 Harley St., W. 1, London.
Secretary: Dr. E. I. Lloyd, 33 Wimpole St., W. 1, London.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Frederic W. Schlutz, Bobs Roberts Hospital, University of Chicago, Chicago.
Secretary: Dr. Alfred A. Walker, Highland Plaza Apartments, Birmingham, Ala.
Place: Milwaukee. Time: 1933.

American Academy of Pediatrics

President: Dr. John L. Morse, 319 Longwood Ave., Boston.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.

American Child Health Association

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. Philip Van Ingen, 125 E. 71st St., New York.

American Hospital Association, Section on Children's Hospitals

President: Dr. Thomas B. Cooley, 7815 E. Jefferson Ave., Detroit.
Secretary: Miss Bena M. Henderson, 721 N. 17th St., Milwaukee.
Place: Detroit. Time: September 12-16, 1932.

American Pediatric Society

President: Dr. Oscar M. Schloss, 1185 Park Ave., New York.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid, St. Louis.
Place: Washington, D. C. Time: May 8-10, 1933.

Association of American Teachers of the Diseases of Children

President: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Secretary: Dr. Oscar Reiss, 1930 Wilshire Blvd., Los Angeles.

Canadian Society for the Study of Diseases of Children

President: Dr. G. A. Campbell, 164 Metcalfe St., Ottawa, Ontario.
Secretary-Treasurer: Dr. L. P. MacHaffie, 162 Clemow Ave., Ottawa, Ontario.

Society of Pediatric Research

President: Dr. Bengt Hamilton, University of Chicago, Chicago.
Secretary-Treasurer: Dr. Charles F. McKhann, Harvard Medical School, Boston.

SECTIONAL

Central States Pediatric Society

President: Dr. Frank C. Neff, 406 W. 34th St., Kansas City, Mo.
Secretary: Dr. A. H. Parmelee, 715 Lake St., Oak Park, Ill.
Place: Kansas City, Mo. Time: October 7-8, 1932.

North Pacific Pediatric Society

President: Dr. Herbert E. Coe, 509 Olive St., Seattle.
Secretary: Dr. Raymond H. Somers, Cobb Bldg., Seattle.

Southern Medical Association, Section on Pediatrics

Chairman: Dr. Horton Casparis, Vanderbilt University Hospital, Nashville, Tenn.
Secretary: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville, Fla.
Place: Birmingham, Ala. Time: November 16-18, 1932.

STATE

Alabama Pediatric Society

President: Dr. Thomas J. McElhenney, 1722, 2nd Ave., Bessemer.
Secretary-Treasurer: Dr. John W. Simpson, 1117 S. 22d St., Birmingham.

Georgia Pediatric Society

President: Dr. M. Hines Roberts, Atlanta.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.

Louisiana State Pediatric Society

President: Dr. Cecil O. Lorio, 245, 3d St., Baton Rouge.
Secretary-Treasurer: Dr. Maud Loeber, 3503 Prytania St., New Orleans.

Medical Society of State of New York

Chairman: Dr. Adolph G. G. De Sanctis, 12 E. 11th St., New York.
Secretary: Dr. G. C. Sincerbeaux, 6 William St., Auburn.

Nebraska Pediatric Society

President: Dr. H. B. Hamilton, 434 Aquila Court Bldg., Omaha.
Secretary: Dr. George L. Clark, 1817 Vinton St., Omaha.
Place: As announced by committee. Time: Second Thursday of each month from October to June, inclusive, 6 p. m.

North Carolina Pediatric Society

President: Dr. Yates W. Faison, 121 W. 7th St., Charlotte.
Secretary: Dr. E. K. McLean, 121 W. 7th St., Charlotte.
Place: Various children's hospitals. Time: Twice a year.

Oklahoma State Pediatric Society

President: Dr. Clark H. Hall, 117 N. Broadway, Oklahoma City.
Secretary: Dr. M. J. Searle, 108 W. 6th St., Tulsa.

South Carolina Pediatric Society

President: Dr. T. D. Dotterer, 1512 Marion, Columbia.
Secretary-Treasurer: Dr. Julian P. Price, 117 W. Cheves St., Florence.

Texas Pediatric Society

President: Dr. Boyd Reading, 2201 Avenue D, Galveston.
Secretary-Treasurer: Dr. F. W. Haehn, Medical Arts Bldg, Waco.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. St. Geo. Grinnan, 925 W. Grace St., Richmond.
Secretary-Treasurer: Dr. J. B. Stone, 2042 Park Ave., Richmond.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. George M. Lyon, 955, 4th Ave., Huntington.
Secretary: Dr. M. F. Petersen, 1013 Quarrier St., Charleston.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. J. E. McClelland, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. P. G. Albrecht, 2009 Adelbert Rd., Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

Secretary: Dr. Lawrence Murray, 1870 Bloor St., W., Toronto.
President: Dr. Gladys Boyd, 56 DeLisle St., Toronto.

BRONX PEDIATRIC SOCIETY

President: Dr. Henry M. Eisenoff, 1018 E. 163rd St., New York.
Secretary: Dr. Morris Gleich, 9 Post Ave., New York.
Place: Concourse Plaza, 161st St. and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

BROOKLYN PEDIATRIC SOCIETY

President: Dr. Irwin Schiff, 658 Eastern Parkway, Brooklyn.
Secretary: Dr. Louis A. Koch, 62 Pierrepont St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Archibald L. Hoyne, 25 E. Washington St., Chicago.
Secretary: Dr. Bert I. Beverly, 8 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

DALLAS COUNTY PEDIATRIC SOCIETY

President: Dr. Gordon B. McFarland, Medical Arts Bldg., Dallas, Texas.
Secretary: Dr. Harold T. Nesbit, Medical Arts Bldg., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

DETROIT PEDIATRIC SOCIETY

President: Dr. Bernard Bernbaum, 5057 Woodward Ave., Detroit.
Secretary: Dr. Sarah S. Schooten, 5057 Woodward Ave., Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

FULTON COUNTY MEDICAL SOCIETY, PEDIATRIC SECTION (ATLANTA, GA.)

Chairman: T. Bolling Gay, 384 Peachtree St., Atlanta.
Secretary: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Place: Academy of Medicine, 32 Howard St. Time: Second Thursday of each month from October to April, 8 p. m.

Memphis Pediatric Society

President: Dr. William R. Graves, 1193 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry J. Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

Milwaukee Pediatric Society

President: Dr. G. H. Fellman, 231 W. Wisconsin Ave., Milwaukee.
Secretary: Dr. George F. Kelly, 161 W. Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. Lewis Webb Hill, 319 Longwood Ave., Boston.
Secretary: Dr. Gerald Hoeffel, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. John Caffey, 50 Haven Ave., New York.
Secretary: Dr. Harry Bakwin, 132 E. 71st St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northern California Pediatric Society

President: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Secretary-Treasurer: Dr. Lloyd Hardgrave, 384 Post St., San Francisco.
Place: Various teaching schools. Time: Monthly.

Northwestern Pediatric Society

President: Dr. Irving McQuarrie, Dept. Pediatrics, University of Minnesota, Minneapolis.
Secretary: Dr. Alexander Stewart, 459 Lowry Medical Arts Bldg., St. Paul.

Philadelhia Pediatric Society

President: Dr. John P. Scott, 2040 Pine St., Philadelphia.
Secretary: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala-Cynwyd, Pa.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. David H. Boyd, 200, 9th St., Pittsburgh.
Secretary: Dr. Theodore O. Elterich, 724 Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. John S. Weitzel, 3103 W. Franklin St., Richmond, Va.
Secretary-Treasurer: Dr. W. E. Chapin, 922 Floyd Ave., Richmond, Va.
Place: Retreat for the Sick, 2621 Grove Ave. Time: First Thursday of each month (other than during the summer).

Rochester Pediatric Society

President: Dr. S. W. Clausen, Strong Memorial Hospital, Rochester, N. Y.
Secretary: Dr. F. W. Bush, 29 N. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month from October to May.

Rocky Mountain Pediatric Society

President: Dr. C. H. Platz, Fort Collins, Colo.
Secretary: Dr. R. H. Verploeg, 1850 Gilpin St., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month from September to May, inclusive, 2:30 p. m.

St. Louis Pediatric Society

President: Dr. Hugh McCulloch, 500 Kingshighway Blvd., St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, Beaumont Bldg., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

Seattle Pediatric Society

President: Dr. C. L. Smith, 1215, 4th Ave., Seattle.
Secretary: Dr. N. W. Murphy, 515 Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 7 p. m.

Southwestern Pediatric Society

President: Dr. Donald K. Woods, 2545 4th Ave., San Diego, Calif.
Secretary: Dr. Jeanette Harrison, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Henry G. Poncher, 5325 Kenmore Ave., Chicago.
Secretary: Dr. John P. Parsons, 320 S. Division St., Ann Arbor, Mich.
Place: Ann Arbor, Mich. Time: November, 1932.